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THE IMPORTANCE OF FILTRATION AND SUPERIORITY OF PURE GAMMA RADIATION IN THE RADIOTHERAPY OF MALIGNANT TUMORS[1]

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THE first attempts to utilize radium in therapeusis and experimentation were made without any importance being attached to filtration. The question was to determine the properties of a new substance. Those who were so fortunate as to possess a parcel of this substance used it in the form in which it had been supplied to them. The filtration was generally limited to the glass wall of the container in which the precious radium was sealed. It was with such a glass tube that, at the instigation of Pierre Curie and with radium furnished by him, Danlos (4) made the first attempts at treatment.

In order to use more efficiently the very small quantities of radio-active substances then available, Strebel (26) originated the idea of placing the radio-active units in the very substance of the tumors to be destroyed, the introduction being carried out by means of a trocar. Among other advantages, the author attributes to this technic those of respecting the integrity of the skin and mucous membranes, of allowing prolonged irradiation, and of utilizing to better advantage the soft, and especially the beta rays.

Another ingenious procedure which enabled one to use a larger proportion of rays and even some of the alpha rays, was conceived by Pierre Curie and first employed by Danlos (3). This consisted in spreading the radium salt on a small, flat, metallic surface and fixing it there with a varnish. The object then sought was to make available as much as possible of the energy furnished by the radio-active substance.

ADOPTION OF FILTRATION FOR UNITS OF RADIUM SALTS

To the preceding conception, which was generally admitted for several years, came to be opposed that of Dominici, which was the fruit of physical and biologic experimental investigations. As early as 1907 this author (9) attributed to the very absorbable rays the necroses so frequently observed at the site of application and to the penetrating gamma rays the principal curative action; he proposed to separate these two groups of radiation by filtration. He wrote: "The results of this technic demonstrate that gamma radiation of low intensity, acting for a long time, can bring about the rapid regression of malignant tumors by avoiding all tissue changes other than those occurring in the tumor."

His experiments, carried out in collabora-

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 28 to Dec. 2, 1927.

tion with Barcat, confirmed his conception (10.) The application for a few minutes, to the surface of the skin of guinea pigs, of a radium plaque containing 25 milligrams of radium sulphate and emitting a composite radiation, provoked a superficial ulceration of the epidermis, followed by the permanent loss of hair and pigment. If the irradiation is prolonged a few hours the necrosis extends to the true skin; such treatment perforates the ear of a rabbit like a punch. Application for 48 hours causes degeneration of muscles, tendons, nerves, cartilages, bones, and ligaments; when repair takes place, these lesions result in permanent dystrophy, muscular atrophy, retraction of tendons, chronic neuritis, articular ankylosis, etc.

On the contrary, if we employ the same radio-active source, but purify the radiation by filtering it through 0.5 mm. of lead, the irradiation may be prolonged for 3 days with impunity, and will provoke only a superficial lesion in the form of temporary loss of epidermis and of hair; and this without modifying the distant action on the ova or seminal cells.

Dominici attached the term "infra-penetrating" to an unfiltered, and therefore composite, radiation, containing besides gamma rays a large proportion of beta and even of alpha rays (according to the model of his apparatus). He called "ultra-penetrating" a radiation filtered through 0.5 mm. of lead containing especially gamma rays and a small proportion of hard beta rays.

These ideas were not admitted without contestation. The long duration of irradiation by means of filtered rays, and especially the resulting loss of efficiency, were advanced as objections to Dominici's proposal. Since, according to Wickham and Degrais (27), the beta rays play the chief rôle in radium therapy, and give to radium radiation its distinguishing feature, to eliminate the beta rays was to rob radium of three-fourths of its value. Delbet (6) advocated the use of tubes deeply embedded in the tumor, considering that the alpha and beta rays only could be useful and that there was no good reason for not making use of this principal energy of radium.

Dominici (11) replied to these arguments that, on the contrary, gamma irradiation alone could act electively and consequently efficaciously on cancer cells, because sarcomatous and epitheliomatous tissue 5 mm. thick was sufficient to greatly reduce the composite radiation. He wrote: "The alpha rays do not penetrate deep tumors; the beta rays barely reach them and are absorbed in their superficial layers, while the gamma rays pass completely through the neoplastic growth and even beyond it. The alpha and beta rays are, therefore, useless and dangerous."

This fact, discovered and demonstrated by Dominici, became a rule of action during the next few years. Radium plaques disappeared little by little from the therapeutic arsenal against cancer and a minimum filtration of 0.5 mm. of platinum became, so to speak, the rule for the units so commonly employed in the radium treatment of cancerous tumors.

RADON UNITS IN THE TREATMENT OF CANCER

Some ten years later, however, the same problem which had been the object of so much discussion in connection with units of radium salts was to be renewed under essentially similar conditions and to be maintained by the same arguments in connection with radon units.

The work of Ramsay and Soddy, and especially of Debierne, had made possible the practical and regular extraction of emanation from radium solution, and this method had become widespread. The Radium Institute of London was the first to attempt, as

early as 1911, the routine therapeutic use of radon (21). Experimental investigations with heavily filtered emanation units were undertaken in 1914 (Debierne and Regaud at the Radium Institute of Paris, 5), but these studies had to be interrupted for a period of five years.

In 1914, Joly and Stevenson (16, 25) advocated a new technic, which consisted in introducing into the substance of malignant newgrowths capillary tubes charged with radon and contained within steel needles, and in maintaining such radon units in position for a definite length of time. The thickness of the walls of these needles was not greater than 0.3 mm. of steel, and this brought us back to a composite radiation, and the employment of soft rays was again advocated by these authors as one of the advantages of their method. The method conceived by Duane in 1915 (12) was still more questionable: filtration was entirely suppressed, except the inevitable filtration provided by the thin glass wall of the capillary tubes containing the radon. These very small tubes were to be permanently deposited within the tissues to be destroyed.

The principal arguments in favor of this technic, which was adopted, advocated, and prepared by Janeway (14, 15), were as follows: prolongation of irradiation time; more homogeneous distribution of the dose to the tissues of the tumor as a whole, by virtue of the multiplicity of radio-active units; employment of a small quantity of radio-active substance; limiting its distant action, and respecting the integrity of the adjacent tissues. While these advantages are no doubt incontestable, it is impossible, on the contrary, to accept as a superior result the necrotic action produced around non-filtered radio-active units, such as Bagg (1) observed on the normal as well as on the neoplastic tissues.

On the contrary, experimentation and clinical observation establish the importance of utilizing in the treatment of cancer only highly filtered gamma rays and of extending to the therapeutic use of radon the precepts of Dominici.

EXPERIMENTAL STUDY OF RADIATION NECROSIS BY INSUFFICIENTLY FILTERED RADON UNITS

A series of experiments, undertaken in 1919 at the Radium Institute of Paris, have demonstrated a certain number of facts (17). To enumerate:

(1) The diameter of the zone of necrosis produced in any tissue by introducing into its substance an unfiltered radon unit is not constant; the diameter of this necrotic zone increases with the intensity of the radiation. In other words, the necrosis is the more extensive as the quantity of radon in the tube is larger. Such increase ceases after a certain fixed limit, beyond which the diameter of the necrotic area does not extend, even if the intensity of the radiation is increased.

For example, let us take a bare tube containing 0.70 millicurie and introduce it into the muscle of a rabbit. The caustic action, due chiefly to the absorption of beta radiation, will be perceptible to a distance of 1.5 mm. from the radio-active source; the radius of the necrotic area will be 3.5 mm. if the tube contains 2 millicuries; 6.0 mm. for 8 millicuries, and 8.5 mm. for 30 millicuries. But the necrotic zone will not increase further, even if the initial radio-active charge be considerably increased. It would appear that the radiation causing the necrosis had been wholly absorbed by such a thickness of tissue.

(2) The diameter of the area of necrosis occurring around a *filtered radon unit* (which also increases in proportion to the intensity of the radiation) is the smaller the greater the filtration.

For example, when the radiation from a tube containing 8 millicuries of radon causes

an area of necrosis with a radius of about 6 mm. in the case of a bare tube, this radius will be only 4 mm. with a filter of 0.15 mm. of platinum; 1.5 mm. with a filter of 0.30 mm. The necrosis will no longer be perceptible with a filtration of 0.40 mm. of platinum.

The result is that we may, without causing any immediate necrosis, employ a unit containing 1.5 millicurie of radon, if the filtration is 0.15 mm. of platinum; a unit containing 7 millicuries with a filtration of 0.30 mm.; a unit containing 8 millicuries with a filtration of 0.40 mm.; a unit containing 10 millicuries with a filtration of 1 mm. of platinum, whereas any unfiltered unit will inevitably produce a necrotic lesion, no matter how small its emanation content (within the order of the quantities utilized for therapeutic purposes).

Briefly, it appears that there should be a threshold of action of the rays which produce necrosis. This threshold is reached, in layers of tissue more and more remote from the radon unit, as the intensity of the radiation increases by augmentation of the quantity of the radio-active substance, or as the filtration is diminished. Such an interpretation of the results of biologic observation has been verified by the physical experiments of Madame Lattès (20). These facts can now be regarded as established; they have been confirmed by Failla (13) and by Cutler (2).

We must now deduce from these facts the most practical manner of employing radium radiation. Since the use of unfiltered radon units inevitably produces necrosis, the problem is simply this: What are the disadvantages of tissue necrosis by radium, on the one hand, and, on the other, what are its advantages?

DISADVANTAGES AND DANGERS OF RADIUM NECROSIS

Radium necrosis is the result of a caustic effect on all the tissue elements within a given radius of the radio-active source—an effect which causes the immediate death of these tissues. The destruction occurs under the same conditions regardless of the organ concerned: muscle, subcutaneous tissue, testis, brain, and, as Bagg (1) has shown, rat carcinoma. Not only are the characteristic elements of these organs affected, but also the elements of the general tissues—supporting connective tissue, vessels, and nerves. Naturally, such destruction is irreparable; months are necessary before the differentiated elements which have been thus destroyed can be replaced by fibrous scar tissue.

The consequences of such a lesion may be readily imagined—

(*a*) *On the striated muscles,* for instance, in an organ such as the tongue. The necrosis provokes the permanent destruction of the muscular fibers; the formation of sclerotic foci entails the retraction and functional impotence of the organ.

(*b*) *On the vessels.* The alterations due to caustic radiation are well known. Madame Dobrovolskaia-Zavadskaia (7) has published a detailed study of these changes. In the vessels of small caliber within the cylindrical area of necrosis, there is immediate destruction of the parietal elements and stoppage of circulation by thrombosis. In the arteries of large caliber, the circulation persists in spite of the death of the cells of the various coats. Delayed and serious hemorrhage may result.

(*c*) *On the nerves.* As Madame Dobrovolskaia-Zavadskaia has shown (8), nerves affected by radium necrosis have but a slight tendency to regenerate. Even if the nerves only adjoin the cylinder of necrosis and do not themselves undergo degeneration, the sclerotic process which ultimately encircles them may cause extremely painful neuralgia.

(*d*) *On the bones.* Because of the high atomic weight of their constituent elements

they can be easily injured, even by filtered radiation when strong doses are given. Since the work of Regaud (22) has been reported we know the seriousness of radiation necrosis of bone. Such injury is inevitable when an unfiltered unit of radon is placed in proximity to a bony or cartilaginous structure.

(*e*) *On the skin and mucous membranes.* Destruction of the skin or mucous membranes occurs whenever these structures are included in the zone of action of caustic radiation. The radiodermatitis which results is too well known to require further emphasis.

(*f*) *On the walls of hollow viscera.* The slough which results from the necrosis often produces by its subsequent detachment perforations or fistulas. Vesicovaginal and rectovaginal fistulas have often been the result of the application of unfiltered or insufficiently filtered units.

(*g*) Finally, to these immediate accidents due to cauterization of the tissues by unfiltered units, we must add the infectious accidents—the tissue necrosis produced by radium constitutes a particularly favorable soil for bacterial growth (Lacassagne, 18).

HAS RADIUM NECROSIS ANY ADVANTAGE?

Let us see if it has any advantage which can outweigh the grave disadvantages which have just been mentioned.

(*a*) *Some have been able to maintain that, by accomplishing the destruction en masse of the tumor, the beta rays insure a more certain disappearance of the tumor cells.* Thus formulated, the fact is undeniable. But this destruction, to which the abiotic action of the beta radiation gives a character of certitude, does not extend beyond a centimeter from the unit, at the most. By placing many units a few millimeters from one another, and by distributing them very regularly in such a way as to include in their cross-fire the totality of the tumor, we may be certain of curing a malignant tumor by complete necrosis. But this tumor must necessarily be small, regular in outline, and, so to speak, encapsulated. Unfortunately, these characteristics are rarely found in malignant tumors. Distant infiltration, the projection of cancer cells along the muscular fibers or along the sheaths of neurovascular trunks are common, and are often unrecognizable by clinical exploration. From this has arisen the common precept, fundamental to all therapeutic methods, radiotherapeutic as well as surgical, that the clinically affected territory must be widely removed. Only the technics employing unfiltered radio-active sources should not be allowed to affect apparently healthy tissues.

Let us add that there are many caustic agents, both chemical and physical; but the radio-active caustic is the most dangerous, the most difficult to control, the most expensive of caustics, and there is no good reason for preferring it to the others.

Briefly, if we do not admit the destruction of certain kinds of malignant cells by the elective action of X and gamma radiation, as scientifically established, we should give up the radiotherapy of malignant tumors as manifestly inferior to other therapeutic methods.

(*b*) One may be inclined to consider the *cicatrizing fibrous reaction* which takes place around slightly filtered radio-active sources as an adjuvant to the destructive action on cells of radiation. On the one hand, the vascular lesions may participate in the elimination of the neoplastic cells by suppressing or reducing their blood supply; on the other hand, proliferation of the connective tissue may set up a barrier which opposes invasion by intact cancer cells. We are not concerned here with the discussion of the indirect effects of radiation and their rôle in the stimulation of defense reactions of the organism against cancer; that is the subject of a separate communication.

One cannot deny that local sclerosis can,

in certain cases, play a useful rôle. It can slow up or even arrest the multiplication of certain neoplastic cells which have resisted irradiation and which have become surrounded by proliferated fibrous tissue. It is by such a process that we can explain local recurrences five, ten, fifteen or more years after treatment; obliged to remain quiescent because of the mechanical conditions which have placed them in a fibrous environment certain cells may recover their power of growth if the sclerotic tissue is absorbed.

Anemia of cancer-bearing areas can be only an accessory factor and can act only at limited points. Telangiectasis, which is constant in skin or mucous membranes modified by rays of poor quality or by excessive doses, proves that the circulation is disturbed but not generally reduced. Moreover, it is not established that anemia favors the normal elements at the expense of the neoplastic elements; on the contrary, many facts favor the inverse hypothesis.

Finally, the fibrous reaction which is regarded as a phenomenon of local defense should be considered more correctly as evidence of changes in the vasculo-connective tissues, and it is known that these changes due to radiations are permanent. The result of these changes is a diminution of local resistance to trauma, to cold, and, above all, to bacterial infection; it is to such changes that are due the *late radionecroses,* occurring sometimes several years after irradiation and the prognosis of which is often very grave. (See the work of Lachapele, 19, on this subject.)

We are, therefore, led to conclude that, if the necessity of destroying all the neoplastic cells is one of the dogmas of the radiotherapy of malignant tumors, respect for normal tissues and their maintenance in a state of integrity as perfect as possible should be another dogma complementary to the first.

THE TECHNICS OF RADIUM THERAPY OF MALIGNANT TUMORS BY FILTERED RADIATION

It is not within the scope of this paper to discuss the different technical procedures based on the use of primary gamma radiation. Those in use at the Radium Institute of Paris have been recently reviewed.[2] It is, however, important to show that all the possibilities furnished by the use of unfiltered units and all the conditions of greater efficacy adduced in their favor can be realized by means of correctly filtered units. We shall not discuss the more or less greater ease and simplicity which the respective technics permit; these are points of view which cannot enter into the problem of the cure of malignant tumors.

The models of radio-active units for gamma radiation in use at present are three in number, and we will review rapidly their characteristics and principal uses:

(1) *Needles designed for radium puncture with ultra-penetrating radiation.* This technic, introduced by Regaud, consists in the interstitial introduction and regular distribution in the interior of a tumor and surrounding area, of platinum needles with a filtering wall 0.5 mm. thick. They contain either a radium salt which is sealed in, or a tube of radon which is fixed temporarily in the needle. Providing the charge does not exceed 2 milligrams of radium or 2 millicuries of radon, the filtration used suppresses all radium necrosis in spite of the absence of a secondary filter. The effective length of the unit measures from 15 to 30 mm. as needed. The total diameter of the needle does not exceed 1.5 mm. As many as 10 to 20 such needles can be introduced without damage into an organ like the tongue and remain there for seven days. This technic assures a homogeneous distribution of the

[2]Lacassagne: Communication to the Seventh Italian Congress of Radiology, Naples, October, 1926. Published in *Strahlentherapie,* 1927, XXVI, 507.

dose, the prolonging of the time of irradiation, the protection of normal tissues, and requires only a minimum quantity of radioactive substance. The statistics of results obtained by this technic at the Radium Institute of Paris in the treatment of cancer of the tongue have been recently brought up to date and published by Roux-Berger and Monod (24).

(2) *The tubes designed for radium therapy within cavities through natural channels and for external curietherapy by molded supports.* The thickness of their filtering wall is 1 mm. (at least) or 1.5 mm. of platinum. Their content does not exceed 15 milligrams of radium or 15 millicuries of radon. Here correct secondary filtration is indispensable. These units are used for applications within cavities, and, therefore, are especially useful in the treatment of uterine cancer. When conditions allow, the most satisfactory treatment of cancer of the cervix is carried out by 6 units, half of which are placed in the uterine cavity and half in the vagina, the average irradiation lasting from five to seven days. The statistics of results obtained at the Radium Institute of Paris by this technic applied to cancer of the uterine cervix have been brought up to date and published by Regaud (23).

These same units serve in the radium therapy of cancers of the skin and of deep or subcutaneous tumors. A substance malleable when hot (mixture of paraffin, wax, and sawdust), chosen because it does not emit harmful secondary radiation, serves for the preparation of molded supports, on the surface of which the units are held at a fixed and suitable distance from the skin.

(3) I shall say only a few words about *curietherapy from a distance.* It consists in using a relatively large quantity of radioactive substance as a homogeneous source of radiation, in placing it several centimeters from the skin, and using it much like an X-ray tube.

In the technic, used at the Radium Institute of Paris for more than three years, and employing a unit of 4 grams of radium placed at 10 cm. from the skin, a filtration corresponding to 1 mm. of platinum absorbs the softest components of the gamma radiation and enables the skin to tolerate stronger doses.

The problem of the superiority of pure gamma radiation in curietherapy of cancer can be summed up in two propositions, the proof of which, I believe, I have submitted.

(*a*) The technics with ultra-penetrating radiation furnish, for the treatment of cancer, the same factors of success which composite radiation can offer.

(*b*) Moreover, they have an advantage over the latter which insures their preponderance; they push back to a considerable degree the threshold of radium necrosis of tissue, and consequently permit the safe administration of much stronger doses of radiation with elective action on the cancer elements.

CONCLUSIONS

1. The work of Dominici has established, since 1907, for units of radium salts, the greatest efficacy against cancer cells, and the greatest harmlessness for normal tissues of the gamma radiation obtained with a minimum filtration of ½ mm. of platinum.

2. It has been established experimentally that unfiltered units of radon provoke around themselves a zone of diffuse necrosis of all the tissues; this zone becomes narrower the more one increases the filtration or decreases the intensity of the radiation; beyond a certain thickness of platinum and for a definite intensity, radium necrosis may be completely eliminated.

3. Radium necrosis is the cause of grave accidents: hemorrhage, paralysis, neuritis, bony sequestration, radium dermatitis, perforation, infection. It offers no compensating advantage.

4. The technics of curietherapy with pure

gamma radiation, which offer the same technical possibilities and a greater efficacy in the treatment of cancer than technics with composite radiation, should be preferred to them.

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THE EFFECT OF X-RAYS ON THE GALL BLADDER: EXPERIMENTAL PRODUCTION OF AN X-RAY CHOLECYSTITIS

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DESTRUCTIVE lesions of practically every organ of the body, it would seem, have been produced experimentally by exposure to roentgen rays. However, in reviewing the literature we have been unable to find any reference to a destructive action on the gall bladder. To us it seemed quite feasible that a destructive dose of X-rays might reach the gall bladder during the course of a treatment to the right breast, base of the right lung, or right upper quadrant of the abdomen.

Experimentally, a bacterial cholecystitis has been produced by many investigators, and there is considerable evidence to show that there is a more or less specific strain of streptococcus (1) and *Bacillus coli* which attacks the gall bladder (2). F. C. Mann (3) has produced a cholecystitis in dogs by injecting Dakin's solution intravenously. The reaction following this injection is completed within 24 hours and is very intense, consisting of a breaking down of the capillaries and an infiltration of the gall-bladder wall with blood. Burgess and Ivy (4) have verified the possibility of producing a cholecystitis by this means.

With the idea of determining the possibility of producing an X-ray cholecystitis, we irradiated a series of dogs and are herein reporting the changes effected in the gall bladder after administration of various dosages. Twenty-five dogs, all in good health, were used for this work. There was no special preparation before irradiation. The animals were fixed in the supine position on a board and tilted slightly toward the left. The gall bladder was located topographically by determining a point two finger-breadths above and two finger-breadths to the right of the xiphoid process. A broad focus universal type Coolidge tube was used. A cone having a portal of 5.5 centimeters in diameter was directed toward the area to be irradiated. During the entire series of experiments certain factors were kept constant, *viz.*, a target skin distance of 12 inches, 5 ma., 4 mm. aluminum filter, and 65 kilovolts. It will be noticed that we used a relatively low kilovoltage, but in choosing this factor we were limited by the capacity of our transformer. The variable factor was the time of exposure. Four dogs were irradiated for a period of thirty minutes, four received a forty-five-minute exposure, and seven an hour exposure. Finally, ten dogs were exposed for a period of two hours by cross-firing for a period of one hour from each side of the gall bladder. At intervals of one and two weeks after exposure the dogs were anesthetized with ether and the gall bladders removed for examination immediately. A precaution to be noted at this point was the possibility of producing traumatic changes in the gall bladder. To avoid this, no hemostats or instruments were used in removing the organ except well away from the area under observation.

Experiments were necessary to determine the dosage required to produce a generalized destructive action on the gall bladder. Thus, four dogs were irradiated for a period of one-half hour. One of these was examined after a period of six days and no definite changes were noted in the gall bladder, although there was some suggestion of small petechial hemorrhages in the fundus.

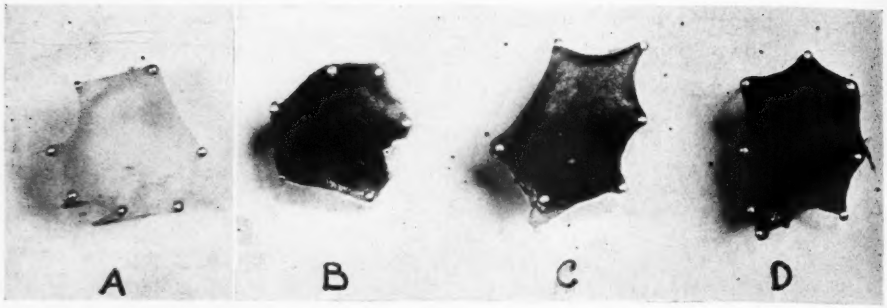

Fig. 1. Typical changes in and gross appearance of the gall bladder after exposure to X-rays. *A*, the appearance of the normal mucosa; *B*, *C*, and *D*, extensive gross changes manifested by changes in thickness and color.

The remaining three animals were examined after a period of twelve days. Two of them showed very definite changes in the gall bladder, manifested by diffuse submucosal hemorrhages in the fundus, which showed a mahogany brown discoloration, but there was no thickening or roughening such as is seen with the characteristic "strawberry" gall bladder, which is the result of an infectious process. Microscopically the blood vessels were seen to be engorged and red blood cells were present free in the submucosa. No changes were noticed in the mucosa, nor was any round-cell infiltration demonstrable in this series.

A second series of four dogs was irradiated for a period of forty-five minutes. Two of these animals were examined at the end of six days and two at the end of twelve days. One in each of the two groups appeared entirely normal, while the other one in each group showed changes similar to those produced in the dogs of the first series. The point of interest in this group is, however, that we had apparently produced definite pathologic changes in the gall bladder with this dose within a period of six days. From these preliminary data we felt that a sixty-minute exposure with the factors given above should produce definite changes in the gall bladder quite constantly. Seven dogs were irradiated for a period of an hour. Two of these were examined at the end of a six-day period and definite hemorrhagic changes as noted above were found in both gall bladders. The remaining five dogs were examined after a twelve-day period and all of the gall bladders showed hemorrhagic infiltrations of varying degrees. Two of the gall bladders showed evidence grossly of a subserous extravasation of blood as well as submucosal hemorrhage. Finally, a series of ten dogs was irradiated for a period of two hours and the gall bladders examined after a period of twelve days. In these gall bladders the changes were of an extreme degree. Grossly they were thickened, apparently as the result of an inflammatory edema. The serosa, although smooth and glistening, showed subserous ecchymotic areas of varying sizes. There was a variation in the color of the mucosa from a dusky brown to a black, and the appearance was that of a severe inflammatory process in which edema and hemorrhage were the predominating changes. Microscopically the epithelium was seen to be swollen. There was a granular deposit in the cytoplasm, and an increased retention of stain in the nuclei, which appeared enlarged. In many areas there was a complete destruction of the epithelium, leaving the connective tissue bare. The connective tissue fibers were widely separated by an edematous exu-

date, the blood vessels were engorged, and there was a very marked extravasation of blood cells. In addition, there was an extensive round-cell infiltration. The picture here that those animals in which the pathologic changes were definite and marked showed certain changes in behavior by which we were quite constantly able to pre-

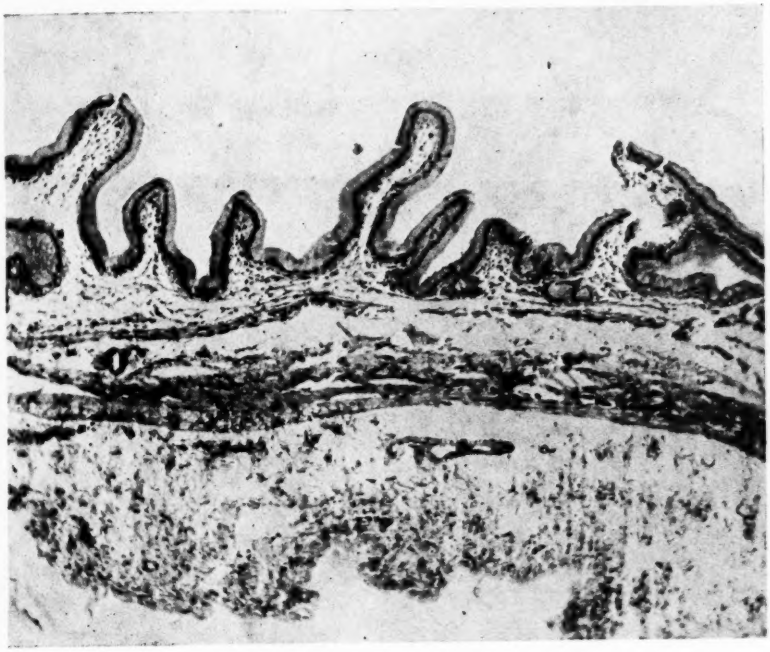

Fig. 2. Microscopical section through a normal gall bladder showing the normal thickness of the various layers and the normal rugæ and epithelium.

in general was that of a very intense inflammatory reaction (Figs. 1, 2, and 3).

It is of interest to note here that in all of the gall bladders in which changes were noted, these were limited to the fundus, except in the series irradiated for a two-hour period. The neck of the gall bladder apparently escaped injury in those animals that received smaller doses, and there is, therefore, more than a suggestion that the fundus of the gall bladder is more susceptible to the action of X-rays than the neck of the organ. However, in the animals irradiated for a period of two hours the destructive action was so great that the entire organ was involved. It is also interesting to mention dict the operative findings. Thus, these animals were listless, lost weight, and trembled when handled, in a very characteristic manner. In all of our experiments a complete autopsy was made to determine gross changes in other organs. No changes of any importance were noted. It must be remembered in this connection that a cone of 5.5 centimeters diameter, centered as accurately as possible over the gall bladder, was used, and hence the amount of direct, stray, and secondary radiation to the adjacent organs was limited. Nevertheless, it is not reasonable to believe that all the radiation to the liver, pylorus, and duodenum was blocked. In fact, it seems likely that

those parts within the limits of the cone received as much radiation as the gall bladder itself.

Wetzel (5) reports injuries to the liver following irradiation and states that these injuries are the result of the secondary rays and are found only in the left lobe of the liver, supposedly as a result of the poor blood supply to this portion of the organ. Mills (6), in describing the effects of radium on the mouse liver, also reports definite changes and states that there are transient changes in the liver cells resembling cloudy swelling, which appear within one to three hours, but disappear within twenty-four hours. Then there is an early inflammatory reaction which lasts a few days, followed by a late reaction which appears in about fourteen days and persists a long time. These latter changes are manifested by an infiltration of the liver with lymphocytes, connective tissue cells, and polymorphonuclear leukocytes. There is also hyperemia, but no necrosis. On the other hand, Krause and Ziegler (7) noted no liver changes from X-rays in animal experiments carried out to determine this point. In our experiments we also were unable to observe any marked liver changes. Case (8), in a series of patients treated by intensive deep X-ray therapy, discusses in detail the hepatic changes produced and suggests that the hepatic and gastro-intestinal injury incurred during the course of such a treatment is at least an important factor in the production of roentgen sickness. His description of the changes produced in the biliary tract are of special interest in connection with our particular

Fig. 3. Microscopical section of the same magnification as shown in Figure 2. There is an enormous thickening of the submucosa due to edema and extravasation of blood; the serosa is similarly involved; the rugæ are almost completely obliterated and some are buried in the submucosa, and there is destruction of the epithelium in many areas.

problem in that he finds that the bile-duct epithelium is far more susceptible to X-rays than are the liver cells. The changes described in the biliary-tract epithelium are almost identical with those observed by us in the gall bladder. Warren and Whipple (9) find that the epithelium of the intestinal mucosa is particularly sensitive to the short wave length X-rays. With exposures apparently not greater than those employed by us, but directed to the abdomen, they produced severe intoxication, which, if recovered from, left chronic intestinal ulcers in their animals. This latter work was verified by Ivy (10) and his co-workers, who, in the course of an additional study of the effect of roentgen rays on gastric secretion, were able to show that the mucosa of the gastric fundus is also sensitive to exposure to X-rays, but not nearly to the same degree as the intestinal mucosa; in fact, these workers rate the sensitivity of the gastric mucosa as about one-half that of the intestinal epithelium.

Although absolutely no effort was made by us during this experiment to establish the comparative sensitivity to X-ray exposure of the various abdominal organs, still it was interesting for us to note that in spite of the very striking gall-bladder changes which we were consistently able to produce, no duodenal or pyloric lesion of note was ever seen. With a cone such as we used, the portal of which was 5.5 centimeters in diameter, it seems entirely unlikely that we were able to converge our cross-fire upon the animals' gall bladders and to miss the duodenum or part of the pylorus in the exposure. We, therefore, are of the opinion that the gall-bladder mucosa is even more susceptible to this irradiation than the epithelium of the intestinal mucosa. It also seems likely that injury to the gall bladder is a factor not to be neglected in the consideration of the causes of X-ray intoxication.

DISCUSSION

In conclusion, we feel that our experiments warrant the statement that a more or less extensive inflammatory process can be produced in the gall bladder with a dose of X-rays commonly used for therapeutic purposes. The extent of the inflammatory process is dependent upon the dose and reaches a maximum after a period of twelve days. The changes vary from small, isolated petechial hemorrhages to a diffuse edema and an advanced, infiltrated, fibrous cholecystitis. The changes are most marked in, and in a majority of cases are limited to, the fundus of the gall bladder. Those animals in which the changes are most marked behave in a more or less characteristic manner, by which one can predict with considerable certainty the pathology present in the gall bladder. It is entirely within the realm of possibility, as borne out by these experiments, that, in administering deep X-ray therapy to the area of the gall bladder, more or less permanent or transient changes are produced in this organ. In a future publication we hope to be able to report whether these changes are permanent or not and whether there is any interference with the concentrating function of the gall bladder as determined by cholecystography.

SUMMARY

1. A definite acute and chronic cholecystitis was experimentally produced in a series of dogs with dosages of X-rays that are within the range of those used for therapeutic purposes.

2. The changes produced are destructive. They consist of hemorrhage, inflammatory edema, round-cell infiltration, fibrous tissue hyperplasia, and, in some instances, necrosis of the epithelium, and resemble the type of cholecystitis produced by chemical means.

3. Basing our opinion on the relative

lack of injury to the exposed portion of the duodenal and pyloric mucosa, we believe that the gall-bladder epithelium is comparatively more sensitive to roentgen-ray exposure than the other organs in apposition to it.

4. The possibility of injury to the gall bladder following deep therapy in the region of the right upper quadrant of the abdomen must be borne in mind.

We wish to acknowledge with sincere appreciation the co-operation and aid kindly given to us by Dr. A. C. Ivy, of the Northwestern University Medical School, Department of Physiology.

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RADIATION AND ITS USES IN THE TREATMENT OF UROLOGIC NEOPLASMS[1]

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FOLLOWING the discovery of the X-ray by Roentgen in 1895 and radium by the Curies in 1898, two new weapons were added to the armamentarium in the treatment of cancer of the urologic system. Until this time surgery had proved only moderately effective in the treatment of these distressing conditions. However, it remained for Kroenig and Gauss in 1911 to effectively apply the roentgen rays in the treatment of female pelvic disorders by the introduction of their multiple portals of entry and cross-fire method of irradiation. In 1913, Pasteur and Degrais introduced a method of applying radium inside of the bladder, using a Coudé gum catheter. We then had two forms of radiation for combating cancer—the X-rays for surface radiation and radium for treatment in hollow viscuses. Through the efforts of urologists, gynecologists, roentgenologists, and physicists, improved methods of applying the roentgen rays and radium were established and a new era in the treatment of tumors of the urogenital system was begun. After the introduction of radium and the X-ray in the treatment of urologic conditions, more recently diathermy, and still later intravenous injections of colloidal lead, and, at this writing, the injection of cancerous patients with tuberculin, a new chapter is being written in the treatment of cancer of the genito-urinary tract. It is now possible either to reduce a large tumor sufficiently in size for its surgical removal or, in a large number of instances, completely destroy it.

Our opinion is based on the results of the following group of cases treated in the Brady Urological Clinic since the advent of deep X-ray therapy.

Kidney.—Sixty-eight cases of kidney tumors have been studied and 29 have been given deep X-ray therapy, either pre-operative, post-operative, or both.

Ureter.—No primary tumors of the ureter have been treated; only those due to metastasis from bladder and kidney tumors have been dealt with.

Bladder.—Three hundred seven cases of cancer of the bladder have been studied; 152 have received deep X-ray therapy. This does not include the benign but does include the malignant papillomata which have received deep X-ray therapy.

Prostate.—Three hundred fifty cases have been studied; 148 have received deep X-ray therapy, either pre-operative, post-operative, or both.

Urethra and penis.—Thirty-four cases have been studied, 5 of which have received deep X-ray therapy in one form or another.

Testicles.—Twenty-three cases of tumor of the testicle have been studied, of which 16 have received pre-operative or post-operative radiation not only for the tumor itself but for the metastasis in the inguinal and abdominal glands.

In this paper only the diseases pertaining to the male urogenital organs will be discussed.

KIDNEY

Radical operative removal is the method of choice. The tumor should be removed as thoroughly as possible; the perirenal fat and glands should be extirpated. If the tumor extends into the ureter—and even though this may not be demonstrable—as

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, Dec. 2–7, 1928.

much of the ureter as possible should be removed, sufficient, at least, to be certain that the operation is complete. After such a radical removal it has been our custom to radiate the abdominal and thoracic aortic glands and the site of the operation with deep X-ray therapy. If, at the time of operation, it is found impossible to remove all the malignant tissue, radium needles are inserted and often radium element. If the veins of the pedicle are involved, if the vena cava contains a tumor, or if the malignant infiltration is so close to the great vessels that the use of radium (element, needles, or emanation) might be dangerous for fear of causing necrosis and hemorrhage, it should not be used and subsequent radiation should be left entirely to deep X-ray therapy. In some cases, with due care, radium may be inserted into the carcinomatous infiltration in the region of the vascular pedicle with comparative safety, and we have employed this method in several cases. If, however, that amount of malignancy is allowed to remain, it has been our experience that neither radium nor X-ray has proved effective in checking metastasis. The metastases following carcinoma of the kidney occur first in the lungs and then in the bones. In a large percentage of pulmonary metastases, deep X-ray therapy will often cause a rapid disappearance, only to re-occur, however, in some other portion of the body. In perirenal and retroperitoneal tumors, which are usually sarcomatous, the use of radium and deep X-ray therapy has proven of great value. This type of tumor is not infrequent in children. We have seen large masses, the size of one's head, rapidly and completely disappear under deep X-ray therapy alone, in a comparatively short time. One patient has been followed for a period of ten years.

In kidney tumors, it has been our experience that a large majority of them occur in stout, well-nourished persons in whom surgical removal is a difficult technical procedure at best. In this group of cases it has been our custom thoroughly to radiate the tumor before attempting surgical removal. There is hardly one instance in which the shrinkage of the tumor has not been sufficient for later operative removal. I have in mind one case in which a huge inoperable tumor shrank up so completely in four months that the man wore a pad in his side to keep what he referred to as his "kidney" from "wobbling around."

URETER

Tumors of the ureter are highly resistent to radiation of any type and when implantation or metastasis in the ureter has occurred the prognosis is extremely bad; the patient usually dies before any benefit can be obtained from the radiation.

BLADDER

In 1896, Nitze announced an epoch-making advance in the treatment of bladder tumors by the introduction of his ingenious operating cystoscope, but it was not until 1910 that Beer and Keyes introduced simultaneously a method known as "fulguration" in the treatment of bladder tumors. Closely following the introduction of fulguration, Paschkis, in 1911, described the first cystoscopic radium applicator. The instrument was evidently inconvenient and lacked any mechanism for holding the radium in place. Pasteur and Degrais, in 1913, devised a method of treating cancer of the bladder with radium by passing the radium into the bladder, supported in a Coudé gum catheter, but it remained for Young, in 1915, to introduce the cystoscopic radium applicator which could be fixed in place against the tumor. With this, it is possible to place a considerable amount of screened radium against or into a vesical

tumor and to hold the radium in place by means of a clamp attached to the table. Many modifications of these cystoscopic radium applicators have been made. It was soon found necessary to make applications of radium *per rectum* in bladder tumors as well as through the urethra, and for this purpose an instrument for holding the radium against the tumor has been devised.

To successfully treat bladder tumors, it is of paramount importance that a correct diagnosis be made. Neither time nor space will permit a lengthy discussion of bladder tumors, but experience has shown that in order to treat a bladder tumor successfully certain factors concerning that particular tumor must be known. In papilloma it must be known whether the tumor is benign or malignant. In papillary carcinoma it must be decided whether it is infiltrating or non-infiltrating, operable or inoperable, and whether or not metastases are present. Only after these factors have been ascertained can the proper method of treatment be intelligently applied.

We have adhered rather closely to Guyon's classification of bladder tumors, which is based on the mode of their implantation. Epithelial tumors of the bladder wall are divided into the pedunculated, implanted, and infiltrating groups. The pedunculated tumors are, as a rule, papillomata. The implanted tumors are those which spring from the mucous membrane and project into the bladder cavity. The infiltrating tumors are regarded as neoplasms which involve the bladder wall deeply and extensively but which project only slightly into the cavity of the viscus. For our purpose, it has seemed that Guyon's classification of epithelial tumors of the bladder offers the selection of the appropriate method of treatment for any particular type of tumor.

The above classification and the diagnosis are usually founded on the gross and cystoscopic characteristics of the tumor rather than on the histologic structures, but, when possible, tissue is also removed for histologic study. Experience has shown that a form of treatment may be effective in one type of tumor but useless in another. In papillomata, fulguration has been the method of choice. It yields results which cannot be even approximated by the most radical surgery, but, on the other hand, it has been found practically useless in the treatment of carcinomata.

The location of the tumor plays an important rôle in its successful treatment. In papillary carcinomata, especially the non-infiltrating or superficial infiltrating type, a combination of fulguration and applications of radium, employing a cystoscopic radium applicator, has proved satisfactory, but in a large majority of these cases it is extremely difficult to determine whether a tumor is superficially infiltrating or not. If it is, it has been our method to supplement fulguration and radium with deep X-ray therapy. In the infiltrating carcinoma with ulcerations in the bladder, this has been the method of choice. When the tumor is so situated in the bladder that it can be resected radically, such is the method of choice. In tumors situated in the vertex of the bladder, radical removal is the method of choice even though part of the peritoneum must be removed. In growths on the anterior, posterior, and lateral walls, radical removal may often be carried out successfully even though the carcinoma is of considerable size. When the carcinoma involves the neck of the bladder, the trigone, ureteral orifice, or prostate, radical surgery, in our hands, has not proved successful, and when it is necessary to transplant the ureter we have found that the tumor had penetrated so deeply that metastases were either present or occurred promptly. In such cases, instead of extensive resections, with ureteral transplantation, a better method of attack is to expose the tumor through the suprapubic

opening, remove the transvesical portion with the cautery, and implant thoroughly screened radium needles in the base. In our experience, thoroughly screened radium needles from 0.5 mgm. to 1 mgm. are preferable to emanations and should be introduced sufficiently close to each other to supply 1 mgm. of radium element per cubic centimeter of tissue. When the ureter has been invaded this method has made it possible to avoid transplantation of the ureter and thus prevent the ascending infections and strictures which have usually followed the latter procedure and which lead to more or less complete destruction of the kidneys. When the carcinoma of the bladder involves the prostatic orifice or deeper portions of the prostate, providing the trigone and remainder of the bladder are free, Young's radical removal of the prostate and seminal vesicles, with anastomosis of the membranous urethra to the anterior wall of the bladder, may be successfully carried out, and is preferable to radium and deep X-ray therapy. When, however, the carcinomatous process has surrounded the neck of the bladder more extensive palliative procedures—such as radium, fulguration, and deep X-ray therapy —are of value.

The amount of radium given should vary with the individual case. In small tumors 600 to 1,200 mgm. may be sufficient after the pedunculated portion of the tumor has been destroyed. The application of 600 mgm. of radium to the pedicle or base of the tumor generally suffices. In large tumors much more may be necessary, and we have found that it is well to alternate radium with deep X-ray therapy. We make it a rule to have these patients return frequently for cystoscopic examination — every six weeks at first and then at intervals of two, three, four, and finally six months. Without alarming them we try to impress them with the importance of early recognition and probable successful treatment of any recurrence. As a rule, they are eager to return to obtain the assurance that all is well. Besides numerous cases in which, up to the present time, the cure has seemed permanent, in many hopeless cases palliative results, especially the cessation of hemorrhage or a diminution of obstruction or irritation, have been obtained.

We are convinced that these methods are far superior to suprapubic operative attacks in such cases. There is no mortality as a result of the treatment, whereas the death rate following bladder resection, especially when the base, trigone, or ureteral orifice is involved, is often very high.

PROSTATE

Only the cases of carcinoma of the prostate that cannot be radically and completely removed surgically, with hope of cure, should be treated by deep X-ray therapy and radium. Where possible, the radical operation—resection of the prostate, seminal vesicles, and trigone—should be carried out. Unfortunately, in a large percentage of cases extension to surrounding tissues and metastases to bones have already occurred, or the disease has progressed so far that complete removal appears impossible. In our experience a combination of radium and deep X-ray therapy has proved the treatment of choice.

Cancer of the prostate can be reached with comparative ease by both the X-ray and radium. If radium is employed, it can be introduced through the urethra with the modern cystoscopic radium applicator, through the rectum by the radium rectal applicator, and through the perineum by needles or emanations. The method we have employed has been similar to the one used in the treatment of bladder tumors. The radium is placed in the desired spot under the direction of a gloved finger in the rectum and held there by means of a clamp

which is attached to the table. The instrument we now use carries two small platinum tubes each containing 100 mgm. of radium element, held tandem in a hollow beak surrounded by silver and gutta percha, which filter out almost entirely the alpha, beta, and secondary or surface rays. Each application of radium is given to a different portion of the tumor, and in some instances we have been able to give as high as 2,000 milligram hours *per rectum* without causing a burn. We do not, however, recommend giving this much radium. Not infrequently irritation, edema, and rectal pain occur after a few treatments, and great care must be employed in applying the radium in order that the radiated areas may not overlap. The same instrument used for applying radium *per rectum* is also used for application in the posterior urethra. By passing this instrument into the bladder it may be turned downwards so that the radium will lie against the trigone and thus afford radiation to the region above the prostate and seminal vesicles. In such cases, the clinical improvement is often amazing. Hematuria and difficulty of urination disappear early. Pain due to metastasis, in almost every instance, will be diminished or completely relieved. We have seen patients leading catheter lives discontinue the use of the catheter after the third day. I have in mind a man weighing over 300 pounds, with an extensive inoperable carcinoma without metastasis, who had been leading a catheter life for almost two years, discard the catheter after the second treatment. At the end of two years he was still in good shape.

The plan of treatment is usually as follows. The patients are treated on alternate days with radium and X-ray, rarely being given both the same day. The radium is given, in rotation, through the rectum, urethra, and bladder. This is done in order to avoid a burn. The number of radium applications varies with each case and the extent of the involvement plus the idiosyncrasies of that particular patient. As a rule, the patient will stand from 400 to 600 mgm. *per urethra,* from 400 to 800 mgm. through the bladder, and from 800 to 1,200 mgm. through the rectum. The treatments usually last for one hour, but if the patient is not able to stand a treatment of this duration, it is given for as long a period as he can stand it. The deep X-ray treatments are given on the days the patient does not receive radium. After the patient has completed the course of radium treatments, daily X-ray treatments are given.

When the diagnosis of cancer of the prostate can be made sufficiently early, radical operation is the method of choice. Our records show over 60 per cent of patients alive and apparently well five years after leaving the hospital. It can be said positively that the treatment of cancer of the prostate has become much more satisfactory in recent years. It is possible to cure now, radically, a certain number of these cases, but in the others by the use of deep X-ray therapy and radium remarkable amelioration of symptoms and arrest of the progress of the disease can be obtained. When complete obstruction to urine is present a conservative perineal prostatectomy will give normal urination. X-rays and radium have contributed more to the treatment of carcinoma of the prostate than any other therapeutic means. Sarcoma of the prostate and adnexa may be very successfully treated by radium and X-ray therapy. We have three patients alive four, seven, and eight years, respectively.

URETHRA AND PENIS

Fortunately carcinoma of the bulbous and pendulous urethra is very rare, especially of the bulbous portion. Carcinoma of the pendulous urethra usually involves the penis, and the treatment is the same. In cases of

the penis, treatment is entirely surgical, if not too advanced, and it should consist of radical amputation of the penis and removal in one piece of the glands of both groins and the tissues surrounding the lymphatics running from the penis to the groins. Our experience does not justify total emasculation nor does it warrant the transplantation of the urethra to the perineum. For those cases in which surgery of one type or another is not possible deep X-ray and radium is the only method of treatment, but it has been almost totally ineffective. One would ordinarily expect excellent results in treating an organ so easily reached. In a few cases we have seen remarkably good temporary results only to be followed by rapid dissemination of the disease, and death.

TESTICLES

Tumors of the testicles (seminoma, teratoma, sarcoma) have proven remarkably resistent to radiation, but a remarkable thing about these tumors is the susceptibility to radiation of their metastases. Undoubtedly surgical removal of the testes should be carried out. There is a great diversity of opinion concerning the radical removal of the retroperitoneal glands and abdominal aortic glands by surgery, or their treatment by deep X-ray therapy. It is our feeling that these glands should be removed surgically and this procedure followed by vigorous and repeated courses of deep X-ray therapy. We have a few cases, so treated, extending over a period of several years—one nine years in which the glands were involved by the metastatic process. In every one of our cases we have followed surgical treatment by deep X-ray therapy. We have two cases in which masses in the abdomen, as large as apples, disappeared under this form of treatment, and the patients are both well at this writing, two years later.

CONCLUSIONS

An attempt has been made in this paper to present in brief the rôle played by radium and deep X-ray therapy in the treatment of genito-urinary neoplasms.

Statistics have been purposely omitted, and in their place have been substituted our methods and opinions of treating these tumors, based on the results of a critical statistical survey of a large series of malignant tumors of all kinds.

BONE TUMORS[1]

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IF progress is to be made in the management of patients with bone tumor, it will be necessary to undertake their treatment in an earlier stage than most of us have had the opportunity to do in the past. With this thought in mind, we reviewed early this year our collection of ninety-two bone tumors. We had three purposes in mind: First, to see at what period in the history of the disease the patients received adequate diagnosis; second, to make a diagnostic analysis of each lesion in an effort to compile the characteristic diagnostic facts about bone lesions that could be applied to individual cases to simplify and make more accurate the diagnostic procedure, and third, to see if there were any leads to be picked up that would help in the post-diagnostic management of these patients.

It was observed that many months usually elapsed between the time, according to the history, that attention was directed to the site where the tumor later appeared and the time a definite diagnosis was made. The point is made and widely accepted by many well informed men that a tumor should be considered as having been at one time a local lesion, the time required for it to become a systemic disease being variable, but usually a period of sufficient length to warrant the belief that earlier local treatment might have given greater promise of permanent cure.

One consideration that brings confusion into the picture is the association of injury with the early history of bone lesions. I make no effort to estimate the importance of trauma as a factor in the etiology of bone tumors. Yet, it is frequently this turn in events that is most conspicuous in the mind of the patient when he relates the history of his complaint. Since injury is common, and uneventful recovery is the usual order, these individuals are justified in their opinion that the condition is trivial at the time. In our analysis of the situation we have come to believe that the family physician whom most of these patients first consult is not alert to the eventualities in bone lesions. During the last few years the general profession has been aroused to a more diligent interest in tumors of the breast, so that, from a number of centers, a feeling of progress is manifested in handling these patients. I am attaching to this presentation a few case histories which seem to me to indicate a lack of that quickened consciousness on the part of some physicians with regard to bone tumors compared to their management of tumors located elsewhere.

After repeated review of our cases in an effort to make a chart similar to one published by Holmes (1), which does not meet our needs, we found that we had about as many rules for diagnosis as we had examples of lesions. For the most part the benign tumors offered little difficulty. Our collection contains thirty-three cases of osteomata and exostoses, eight of osteitis fibrosa cystica, six of chondroma, three of myositis ossificans, and one of extensive calcified subperiosteal hemorrhage. The giant-cell tumors, of which there are five in this collection, offered the most factors leading to confusion in their analysis of any in the group. Twenty-four cases of metastatic bone lesions were not difficult, because in

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, December 3–7, 1928.

most instances definite histories of primary malignancy and pulmonary metastases were available.

Among the twelve cases of primary malignant bone lesions is one of multiple myeloma which is fairly typical. It was in the remaining eleven that our diagnostic chart became unwieldy. Review of the microscopic reports from the pathologists in the cases in this group caused great confusion. In no two instances was the terminology the same, and in only a few was it possible to determine accurately the opinion of the pathologist with regard to the degree of malignancy.

Having arrived no place in particular by these efforts I turned to the literature of the last decade. From its earnest study it appears that the surgeon, the roentgenologist, and the pathologist constituted a triumvirate that wrought confusion in skeletal oncology from which the medical profession will not recover for many years. The first practical step toward clearing up this confusion from a clinical standpoint was the establishment of the Registry for Bone Sarcoma by the American College of Surgeons at the instance of Codman (2, 3), accounts of which were published in 1922 and 1925. The terminology and classification recommended by the Registry is simple, reasonable, and adequate at this point in the development of the subject, and should not be tampered with by the great or near-great until further definite and valuable knowledge has been gained. The most recent extensive contribution to this subject and perhaps the most valuable of any made up to this time was the analysis of bone Registry material reported by Kolodny (4).

One serious effort on the part of the pathologists to clarify the atmosphere with regard to their contribution to the management of patients with bone tumor was the work of MacCarty (5), reported to this Society at its meeting in Milwaukee in 1926. A similar basis of tumor analysis as presented by MacCarty, if generally adopted, would be of more material service to the surgeon in making a prognosis in these cases than any other method that has come to our attention. The facts set forth in his discussion of the pathogenesis of bone tumors are widely accepted, and his study of a great many specimens and the correlation of microscopic information with the clinical progress of many patients give strong support for the promise offered by this type of analysis. If one seriously investigates the pathologic reports from microscopic study of bone tumors in the past decade, he will still be faced with the necessity of making his own interpretation of what the pathologists mean.

In the light of our experience and following that of others, I have come to the conclusion that for practical clinical purposes the roentgenologist should submit to his consulting surgeon a carefully written opinion as to whether a bone tumor is benign or malignant, eliminating therefrom all efforts to make a refined diagnosis that will probably get him into a close place, if it does not bring him into actual disrepute. This diagnosis should be based on all available information—historical, clinical, physical, as well as radiological. It has been our custom to give such an opinion for clinical purposes. However, further analysis is always interesting, so we maintain for our private amusement a "stunt file" in which we indulge in a bit of diagnostic gymnastics according to various classifications and terminologies that have been current for many years, although I do not see that these efforts at highly refined diagnosis have ever accomplished any good for our patients or ourselves.

The outlook for treatment of these patients is anything but hopeful, if the practice of the future is not going to improve over that of the past with respect to the period

in the history of the disease at which it is treated. Unless the physician who is first consulted in all of these cases has a much keener realization of the importance of early treatment the outlook is grave, whatever the method. My experience in the X-ray treatment of bone tumors is as limited as that of most radiologists in contact with surgical groups. However, two of our patients had so-called deep roentgen therapy with temporary arrest of the disease and some reduction of pain, and another is now living and well after three years. Recently Kahn (6) reported recovery of a giant-cell tumor after deep X-ray therapy, also remission of symptoms and arrest of growth for a short time in malignant tumors. He presented illustrative material on several cases, showing spectacular results obtained in tumors of unconfirmed diagnosis, and recommended deep X-ray therapy for tumors which are inaccessible for complete surgical removal. The reports of a few others, besides Kolodny in his analysis of the Registry material, and Evans and Leucutia (7) in relation to radiation treatment of bone tumors, appear to hold some promise of a greater degree of future success for this method. I have not such a fatalistic point of view concerning the radiologic management of bone tumors as some of the men who are contributing to the literature. One might dare to suggest that it has been a very short time since any method of approximating the dosage administered to a part has been developed, and, further, it is a known fact that in a large number of the institutions where radiologic treatment is given no adequate instrument for measurement of dosage has been installed. Therefore, it might be remarked again that the dictum concerning the value of roentgen treatment should be withheld until an opinion has been rendered from institutions where adequate control of dosage has been practised on a fair number of patients in whose cases reasonably accurate clinical, roentgenologic, and pathologic diagnosis has been made.

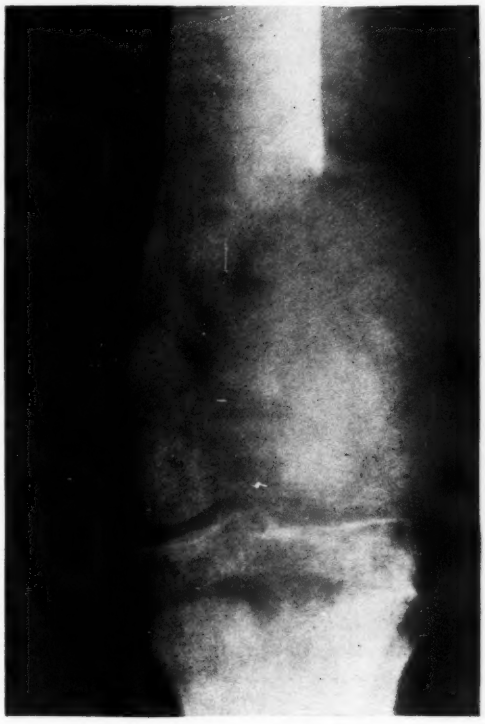

Fig. 1. Case 1.—Osteogenic sarcoma of lower end of femur. The patient consulted physicians early but did not get a diagnosis until too late for treatment.

CASE REPORTS

Case 1.—A ranchman, aged 29, came to the Jackson Clinic November 23, 1922, on account of a swollen knee. In February, 1922, he bumped the side of his left knee on a log and about a month later a tender spot developed at the site of the bump. In May a doctor put on a cast for ten days, then directed the patient to wear an elastic bandage, which he continued to do for five weeks. In August, 1922, he had an X-ray

Fig. 2. Case 2.—Osteogenic osteolytic sarcoma of humerus and ulna at the elbow. The patient did not receive a diagnosis until a year after discovery of bone changes.

examination in Montana but the doctor told him he did not know what the trouble was. In September, after an examination in another small town, a doctor told him he had bone tuberculosis. About the middle of October he was given another diagnosis of osteomyelitis of the lower end of the femur. About this time a section of the tumor was sent to an eminent pathologist, who reported a diagnosis of giant-cell osteosarcoma, with a note that the tumor appeared to be a little more actively growing than this type of giant-cell tumor usually is, and hence more malignant.

The patient was referred to our roentgenologic department for examination of his knee, which was intensely swollen and tender, motion being limited on account of pain on manipulation. An X-ray examination revealed extensive destruction of the lateral condyle and lower end of the shaft of the femur by a tumor which had invaded the adjacent soft parts. There was no evidence of new bone formation and definite limits of the extension of the tumor into the soft parts could not be recognized. Diagnosis was made of osteogenic sarcoma. The patient did not have an amputation. He died in June, 1923, of pulmonary metastasis.

Case 2.—A housewife, aged 77, came to the Clinic, April 9, 1928, and was referred to our service because of pain and swelling in the right elbow. In April, 1927, she had fallen and broken her right arm above the elbow. She had consulted a physician, who told her that he could not set the arm because "there was no bone to set." She carried her arm in a sling thereafter. The elbow began to swell immediately after the accident and the pain constantly increased. At the time of our examination a firm nodular mass 15 cm. in diameter was felt on the lower end of the humerus. The patient complained of pain radiating down the arm to the fingers, which was greatly intensified at the least effort to manipulate the elbow. The patient's general condition was fair and showed little evidence of loss in weight. There was moderate increase in local heat but no visible skin changes in the region of the tumor mass. There were moist râles throughout both lungs and pulmonary metastases were suspected on physical examination, confirmed on the X-ray films, the right lung field showing numerous metastatic lesions. X-ray examination of the elbow showed abrupt dissolution of the continuity of the humerus 6 cm. above the elbow joint, below which the entire bone structure was destroyed except a thin shell of the condyles. Almost all of the olecranon process and the proximal 4 cm. of the ulna were destroyed. There was evidence of extensive soft tissue invasion. On the abrupt end of the humerus and upward for 7 cm., the lateral diameter of the humerus

was narrower than normal, as if destroyed by erosion of the lateral aspect, but the cortical margin was smooth and slightly more dense than elsewhere in the bone. X-ray diagnosis of osteogenic osteolytic sarcoma

Figs. 3 and 4. Case 3.—Osteogenic sarcoma. The patient consulted a physician early but diagnosis was delayed several months.

of the lower 7 cm. of the humerus and the proximal 4 cm. of the ulna was made. This patient had an amputation at the shoulder April 11, 1928, at her own request, on account of the pain she had suffered in the elbow. From a microscopic section of this tumor the pathologist reported "a large spindle-cell and giant-cell sarcoma of a type of periosteal origin, a definitely malignant tumor." The patient died June 19, 1928, with extensive pulmonary involvement.

Case 3.—A woman, aged 19, came to the Clinic January 11, 1928, complaining of pain and swelling in the left knee. She first noticed a pain in the left knee in July, 1927, while playing golf. This pain was treated as for a sprain for several months by applications of camphorated oil and bandages, but it increased in severity and localized over the lateral aspect of the leg below the knee, when a plaster cast was applied. The pain was more severe on walking, but there was no limitation of motion. The patient's general appearance was not good; she had lost considerable weight and strength and her appetite was poor. On physical examination her right knee was found to be swollen about Grade II, with exquisite tenderness over the lateral aspect, and there was pain on manipulation. She had had X-ray examinations November 11 and December 20, 1927, at which times she had been told that she had osteitis of the tibia. At the time of our examination (on January 11, 1928), she submitted the films made on

the previous occasions. The first films are poor, but show new bone formation; the second show marked increase of this new bone, with unmistakable evidence of invasion of the soft parts, both laterally and posteriorly. X-ray films made January 11, 1928, revealed mottling and increased density of the upper end of the tibia, with a small amount of increase in new bone formation and soft tissue invasion since the X-ray examination in the previous month. *X-ray diagnosis:* Osteogenic sarcoma of the head of the tibia. After much consultation this patient had an amputation at the middle of the shaft of the femur January 19, 1928. A section of the tissue sent to a pathologist was reported as "a nodular cartilaginous tumor of atypical structure with the peripheral portions showing change into invading spindle-cells. *Diagnosis:* Chondrosarcoma." The cross-section made vertically through the center of the shaft of the tibia showed central bone destruction and tumor invasion throughout the proximal 5 or 6 cm. At the time of this writing the patient is in about the same state of health as preceding her amputation, but there is no evidence of metastasis.

CONCLUSIONS

1. Treatment of bone tumors in the past has been undertaken in most cases late in the disease when it has probably already become systemic.

2. Indifference of general practitioners to the serious probabilities arising from apparently trivial early history of bone lesions often delays correct diagnosis and treatment.

3. Confusion of terminology and classification has interfered for many years with progress in the management of bone diseases.

4. Malignant bone tumors do not usually fit any simple diagnostic scheme of classification; therefore, the best analysis of a bone tumor the roentgenologist can give is an accurate opinion as to whether it is benign or malignant.

5. The value of radiation therapy is as yet undetermined and conclusions concerning it should be suspended until further evidence has been reported.

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DISCUSSION

Dr. H. M. Meyerding (Rochester, Minn.): To you as roentgenologists, this symposium must be of great interest. Undoubtedly the X-ray, with properly prepared plates and with expert interpretation, permits the vast majority of bone tumors to be accurately diagnosed. It seems to me, however, that plates should always be made in two directions, posterior and lateral. I showed, at the Milwaukee meeting of the Radiological Society of North America, two years ago, I think, some 265 cases of osteochondromata in which a fair percentage had been diagnosed as malignant. There should rarely be any excuse for this, as with carefully prepared roentgenograms, properly in-

terpreted, a correct diagnosis should be practically always available in that group of benign tumors. As to a classification of bone tumors, the Sarcoma Registry has given us an excellent one, one with which, however, the members of the committee are not themselves fully satisfied. At the Dallas meeting of the American Medical Association, in 1926, I presented a modification of that classification, beginning with the inflammatory lesions, including in that group of inflammatory lesions the group of osteitis fibrosa cystica, which we may look upon as an inflammatory lesion sometimes associated with trauma. Then we took the group of benign osteochondromata, and we placed the giant-cell tumors next, to separate them from the malignant endotheliomata and sarcomata. I felt that that, as a working classification, would appeal to the average doctor, to whom I was speaking—it seemed to me an understandable classification. Do not forget that while you may be experts in the interpretation of shadows of the bones thrown upon the plate, you must not neglect the clinical side of the picture; you must make yourselves familiar with the findings in bone tumors clinically as well as in the roentgenograms. This will be of great assistance to you, and frequently will make quite obvious the true character of the lesion, whereas the X-ray plate may leave you in doubt.

Now, as to the treatment of the osteitis fibrosa cystica group—I believe it is early surgery. I am not in favor of the "watchful waiting" which has, in the past, been advocated. These cases usually start with mild, rheumatic-like pains, and are frequently first recognized following pathologic fracture. If the contents of the cyst is early removed and the cortex crushed in and the parts kept in good position, union takes place without a great deal of callus. When you determine the fact that there is a bone cyst present, always be sure to make X-ray examination of the other long bones, for not infrequently multiple bone cysts may exist. In the *Journal of Bone and Joint Surgery*, in 1918, I reported cases of osteitis fibrosa cystica which had been diagnosed by good men as sarcoma, and operated upon. Bear in mind that that single cyst should always be looked upon as possible multiple cyst. In several of those cases it happened that all the long bones in one limb were involved. I know of no evidence that radiotherapy does any particular good in this group of cases.

Then let us go on to the giant-cell tumor group, which I feel we should classify as benign. There is evidence that the giant-cell tumor may be treated and cured by X-ray therapy. However, I believe that not only have we the question of cure over a long period of time before us, but we have to consider the economic side of it to the patients. When it is possible to remove the entire tumor by curettage, with or without transplantations of bone, as I have shown in my report, in 1924, before the American Medical Association, I believe it is preferable, as it saves the patient time and money. I think we should stay open-minded and not depend on any one group or any one type of therapy, but, rather, choose the type that is most beneficial to the patient in the shortest length of time. Certain types of giant-cell tumors that come to us we treat surgically, and there are certain types that are not surgical cases because of position, size, etc., which we treat by radiotherapy.

Osteochondroma may occur as a single local tumor or as multiple tumors. As a rule, such cases do not require surgery in the beginning, but, from more recent experience, I would advise the excision of these tumors before they get too large and before they cause deformity, which may be practically irreparable at a later time. Bear in mind also that these tumors may exist for months and years before they are discovered. Sim-

ple excision and cautery to the base of these tumors is the treatment which we advocate, and I have seen no benefit whatever come in this group from radiotherapy. When we come to the periosseous fibrosarcoma group, I believe that excision may be practised, with the implantation of radium needles with some benefit.

The endotheliomata, which resemble osteomyelitis both clinically and by X-ray examination, react marvellously to radiotherapy, and one sometimes makes the false supposition that the condition is cured. However, metastasis usually occurs in the lungs, and especially in the bones of the skull, with fatal termination at a later date.

In the osteogenic sarcoma group, the prognosis has been bad; amputation has been a palliative measure, and radiotherapy has, in our hands, done very little.

Usually in the metastatic tumors such as carcinoma of the prostate and carcinoma of the breast the patients get relief from pain through X-ray therapy, and frequently the size of the tumor is decreased.

I wish, therefore, to again accentuate the value of not only making a diagnosis from the X-ray, but of bearing in mind also the clinical aspects of the case and familiarizing yourself with the findings clinically. As regards treatment, I want to be open-minded; I want to advocate no one definite form of treatment, but, rather, the intelligent selection of one, or a combination of all, after careful consideration as to the local or general character, whether the tumor is benign or malignant, the size of the tumor, the age and sex of the patient, with due regard to his general condition.

Dr. L. T. LeWald (New York): The difference in diagnosis of bone tumors and the method of treatment, I think merits our most careful consideration.

I wish to report two cases for diagnosis and method of treatment. Now, here is a tumor or cystic change, with expansion of the shaft of the bone extending to the epiphyseal line, in a young individual; it shows evidence of swelling and protrusion, due to the bone condition. The case was referred to me by Dr. Reginald Sayre, and he asked me if I would try roentgen therapy. We started the case under moderate voltage, 120,000 volts, and I will show the result. There is gradual improvement, until the cystic condition of the bone has practically entirely disappeared, and, most remarkable of all, there has been a retraction of the expanded portion of the bone, so that, so far as the general appearance goes, there is no evidence of any appreciable swelling. The next slide shows the case just a month or so ago, and we regard the case as a very satisfactory cure. [Shows slide.] There has been no involvement of the epiphyseal region; the growth of the bone is undisturbed, and for this particular case it is a very satisfactory result. Now, as to the exact designation of this case, is it a giant-cell tumor, or would you classify it as osteitis fibrosa cystica? I have asked Dr. Herendeen to see this case with me, and he regards it as a giant-cell tumor. There is a statement made that giant-cell tumor extends farther down, and that is probably the case in an adult—that it extends to the cartilaginous end of the bone. I will now show you a giant-cell tumor in another case, in the shaft of the femur, with less evidence of reticulation, but a similar response to roentgen therapy. I examined the case a month ago and there is still further filling in with good solid bone and some condensation and narrowing of the shaft, so that it more closely resembles the opposite side.

Dr. Sisk (closing): I wish to emphasize the opinion that the diagnosis of a bone tumor should be made in the light of the clinical prognosis, that is, whether it is benign or malignant. Such a diagnosis cannot be

made safely without consideration of the clinical, physical, X-ray, and microscopic evidence. The confusion of the past must be clarified so that the family physician may help his patients with bone tumor to get earlier treatment. The majority of cases show too great delay in management after a diagnosis has been made.

Primary Lung Carcinoma. I. S. Ravdin. Am. Jour. Surg., March, 1929, VI, 337.

The author reports eleven cases of primary lung cancer. The etiology in most cases is obscure, but it has been reported rather frequently in localities where certain metals are mined. He also states that tuberculosis may be an etiological factor.

There are three types of lung cancer, depending on whether they originate in the bronchial epithelium, the bronchial mucous glands, or the alveolar epithelium. These tumors metastasize widely, and the metastases may be found in almost any portion of the body.

The author found cough to be the first symptom in the majority of cases. In those cases with associated bronchiectasis, the expectoration is usually profuse, and the sputum may be blood-tinged. Dyspnea and pain may also be major symptoms.

The roentgen ray is of major importance in the diagnosis of these conditions, and presents shadows that are fairly characteristic. The clinical symptoms and signs are often not characteristic. Occasionally metastatic glands furnish the diagnosis. In two cases the author inserted a large aspirating needle directly into the tumor and obtained small bits of it for microscopic examination.

H. P. Doub, M.D.

STATUS RÖNTGENOLOGIÆ[1]

By PROF. GUIDO HOLZKNECHT, VIENNA

THIRTY-THREE years ago a new star arose on the scientific horizon which threw wonderful rays of unknown nature over the world. These new rays, the discovery of which was due to the persistent and unparalleled efforts of one single man, have revolutionized the whole scientific world with their extraordinary range and vital bearing on life as a whole and science in particular. Their bearings on medicine have undergone such an unprecedented and rapid progress of wide scope and productive nature that they have won a permanent and indispensable place in the world of medicine.

The changes the X-rays have produced are so vital that they are calculated to contribute to the enrichment, improvement, and correction of medicine in all its branches—diagnosis, therapy, and prognosis. These newly discovered rays have also rendered valuable service in research on the subjects of anatomy, physiology, and pathology.

The literature already published about their preliminary and easily comprehensible phases could fill a whole library, but in order to exhaust the subject, a tenfold increase in the present literature would result.

The application of roentgen rays in medicine has developed with such extraordinary rapidity that, to-day, not only specialists of all branches have realized and appreciated their help and great services, but general practitioners also have admitted their indispensable and valuable help, some to a great and others to a less extent.

In the history of roentgen development we perceive two different periods: a short period and a long one.

In the short period it was possible only to diagnose fractures and foreign bodies, while in the long period, with the help of contrast materials, we are able to diagnose the various groups of diseases, and also to treat them, such as hyperplasia, inflammatory and neoplastic conditions.

In that short and early period the technic was difficult, but the diagnosis an easy one.

I will now show two roentgenographs. The one on the left is thirty years old and, as you see, is a very bad one, although to produce it called for a painstaking technic and a tedious process. It required nothing shorter than ten minutes' exposure in the hands of the best assistants and most efficient technicians, although anyone can tell you the diagnosis at a glance. The one on the right is an example of to-day's procedure. Technically it is perfect. The technic has been rendered relatively so easy that any medical man or efficient technician can learn it in one year. The diagnosis is also evidently very clear. It is a fracture—but there is something else besides the fracture that attracts our attention and makes us think that at the site of the fracture and apparently previous to its occurrence there was a lesion which predisposed the bone to break through.

Now, what is that predisposing cause? Is it a sarcoma with its bad prognosis and does the question of amputation arise, or is it a harmless cystic disease or osteitis fibrosa, or, again, is it merely a harmless congenital maldevelopmental condition, or is it tabes? In order to come to a definite and right diagnosis we need vast experience and exact study of hundreds of such cases, and it is only then that we can say that it is a metastatic condition after carcinoma of the prostate. It was not easy to arrive at such a conclusion.

Keen observations of the clinical and

[1]Read before the International Congress on Tropical Medicine and Hygiene, Cairo, Egypt, December, 1928.

roentgenologic picture of the disease, its progress, operation, and postmortem findings, pathologic study and finally physical, roentgenologic, and optical study—I say, all these are necessary factors in our diagnosis. In the history of the numberless works accomplished and valuable researches achieved it was possible to succeed and arrive at a definite result only through small steps and in a piecemeal manner, although the ultimate issue is worth days and nights of persistent work and painstaking study.

Many countries have taken part in the progress of roentgenology and actually contributed to its development, and the names of those who devoted themselves to its study with success are greatly honored and fully appreciated in the world of medicine. France, America, England, Germany, and Austria—these are the nations that have taken the lead in the field of radiology, and are regarded as the pioneers to whom the medical scientific world is greatly indebted and owes its present radiologic progressive status, although in the case of Austria its efforts have been more fruitful and luckily met with more success.

As for my own humble person, I feel greatly honored in having been given this opportunity to address you, and I also consider myself very fortunate in having been able to contribute to the development and progress of roentgenology with something valuable and lasting in the way of organization. I knew, twenty-five years ago, that the technic would be greatly improved and perfected by technicians and engineers, but that development in the diagnostic and therapeutic processes was a gigantic task which could be accomplished only by the medical scientific men themselves.

Now, how were we going to interpret and correctly translate all those thousands of heterogeneous roentgenograms which the roentgen machine could deliver to us in overwhelming quantity?

In my search for a solution of that problem I was impressed by the extraordinarily close resemblance that exists between our problem and others of very much the same nature, in medicine itself, and found better analogy still in industry. I came to the conclusion that in order to accomplish so great a task, two factors are necessary:

(1) The first one is the *division of labor, or specialization,* and the broader the subject the more is the division and subdivision and the further is the specialization.

It may be true that one can master any written branch of science, and in a few years' time can learn all its secrets, but since our life is short, in order to achieve success and arrive at a great and a definite result, one must restrict oneself to a small part of one branch only. I venture to mention this here because the future development of roentgenology is going to be constructed on these lines. When I say specialization, I naturally mean a thorough one, so that it includes and embraces all the neighboring subjects which bear connection to it. Many of my younger colleagues have followed this system and disciplined their studies on these lines, with the result that we have now in Vienna a great number of radiologists who have studied all branches of roentgenology, but amongst whom each one has devoted the best of his energies and abilities of research to one small branch only. This system has produced amongst our roentgenologists in Vienna specialists in different organs and diseases of the body, namely, specialists in the skull alone (including eyes, ears, nose, and nervous diseases), others who have specialized in diseases of the heart and large vessels, others in the mediastinum and tumors of the thorax, or tuberculosis and other diseases of the lungs, or of the stomach and intestines, or of the urinary tract and female generative organs, or of the bone and joint diseases. Thus we have specialists in every branch of medicine who are best

qualified not only in the diagnosis of certain diseases, but also in the application of roentgen therapy as well.

One who restricts himself to a small subject of research can more likely reach the zenith of perfection, as he can see down to the darkest depths and climb up to the highest peaks of knowledge and skill—all others can learn from him and in turn help him.

This, my hearers, is the system of choice for specialization, which has been followed everywhere, and it is the shortest way that insures success and conducts the student to the highest altitudes of perfection.

(2) The second factor which I hold to be vital is *the laying down of good and sound bases and foundations.*

Twenty-five years ago many of the fundamental questions in medicine of the utmost importance were still unanswered: What roentgen rays are; how they pass through the body, and through other receiving and intensifying layers; what is their effect on the body under normal and pathologic conditions; what is the normal picture of any part of the body and which of the changes that occur in that picture are due to technical or photographic causes, which are due to age and constitution of the individual, and which are brought about by disease?

In order to answer these questions careful training and exact study are necessary. Also, their solution necessitates the teaching of the elementary science which forms the basis and foundation of roentgenology, that is, roentgen-physics, roentgen-anatomy, roentgen-biology and physiology, and, further, general roentgen-diagnosis and general roentgen-therapy. Foundation and specialization cannot be separately developed; they must go hand in hand, and must be cultivated at the same time. Research workers in every special branch must create and from their own experiences elicit differences and discussions in these elementary scientific branches and in general roentgenology, and thus partake in and bring about the progress and further development of the latter. Such a system has been tried, and, happily, proven efficient and successful.

STUDIES IN THE DYNAMICS OF HISTOGENESIS[1]

XIV. (A) Experimental Surgical and Roentgenographic Studies of the Architecture of Human Cancellous Bone, the Resultant of the Back-pressure Vectors of Muscle Action. (B) The Remittent Back-pressure Vectors of Muscle Action in Joint Range of Mobilization Determine the Mature Pattern of Cancellous Bone, Not the Immobile Static Pressure of Body Weight. (C) The Clinical Significance of This Study

By EBEN J. CAREY, M.D., Director, Department of Anatomy, Marquette University School of Medicine, Milwaukee, Wisconsin

THE main objectives of this paper are the following: *that the structure of cancellous bone is determined* by the capacity for movement in the chief plane or planes of action at the related joint; *that the structure of cancellous bone related to monaxial, biaxial, and triaxial joints is characteristic and definite* for each type of joint; *that the pattern of cancellous bone is the product* of the remittent back-pressure vectors of muscle action in joint range of mobilization and not the product of the immobile static load of body weight; *that skeletal bone is the product* of an adequate pressure of differential growth,[2] as well as adequate pressure of myogenic function; *that tension although transmitted by bone* is not a trophic stimulus to bone origin; *that by local muscular excision* there is a focal atrophy of corresponding cancellous bone trabeculæ; *that prior to birth there is a growth relativity* leading to a mutual antagonism between the length growth of the femur and the back-pressure of the developing thigh musculature that results in a relative decrease of femoral volume and length, and corresponding to thigh muscular development an increase of femoral density or consolidation and weight. The clinical significance of this study reveals the rôle of action as well as the reciprocal dependency of the muscular and skeletal tissues as mutual maintainers of each other's normal structural integrity and the logical use of a timed early mobilization after rest in the treatment of derangements of the locomotor apparatus, such as fractures and dislocations, advocated by Lucas-Championniere,[3] Hey Groves,[4] Jones and Lovett,[5] Dean Lewis[6] and many others.

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[1]The objective evidence presented in this paper constituted part of a scientific exhibit by the writer at the annual meetings of the following medical societies: The American Association of Anatomists, Ann Arbor, Michigan, April, 1928; American Medical Association, Minneapolis, Minnesota, June, 1928 (awarded silver medal); Wisconsin State Medical Society, Milwaukee, Wisconsin, September, 1928; Radiological Society of North America, Chicago, Illinois, December, 1928 (second award).

[2]Carey, Eben J.: (*a*) Early Stages in the Development of the Pig, with Reference to the Influence of Muscular Activity upon its Ossification. Anat. Rec., 1918, XIV, 1. (*b*) On the Interaction of the Primary Femoral Ossification, Thigh Muscular Differentiation, Knee and Hip-joint Formation during the Period of Rotation of the Hind Limb of the Pig. Anat. Rec., 1919, XVI, 3. (*c*) Studies in the Dynamics of Histogenesis. I—Tension of Differential Growth as a Stimulus to Myogenesis. Jour. Gen. Physiol., 1919, II, 4. (*d*) II—Tension of Differential Growth as a Stimulus to Myogenesis in the Esophagus. Jour. Gen. Physiol., 1920, III, 1. (*e*) III—Growth Motive Force as a Dynamic Stimulus to the Genesis of Muscular and Skeletal Tissues. Anat. Rec., 1920, XIX, 199. (*f*) IV—Tension of Differential Growth as a Stimulus to Myogenesis in the Limb. V—Compression between the Accelerated Growth Centers of the Segmental Skeleton as a Stimulus to Joint Formation. VI—Resistances to Skeletal Growth as Stimuli to Chondrogenesis and Osteogenesis. Am. Jour. Anat., 1921, XXIX, 1. (*g*) Direct Observations on the Transformation of the Mesenchyme in the Thigh of the Pig Embryo (Sus scrofa), etc. Jour. Morph., 1922, XXXVII, 1 and 6. (*h*) The Regeneration of the Patellæ of Dogs. Am. Jour. Anat., September, 1927, XL, 127.

[3]Lucas-Championniere, Just: The Treatment of Fractures by Mobilization and Massage. Brit. Med. Jour., Oct. 3, 1908, II, 898.

[4]Groves, E. W. Hey: Fractures. William Wood, New York, 1922, p. 194.

[5]Jones, Sir Robert, and Lovett, Robert W.: Orthopedic Surgery. William Wood, 1923.
Lovett, Robert W.: After-treatment of Infantile Paralysis. Am. Jour. Orthopedic Surgery, 1917, XV, 687.

[6]Lewis, Dean: Clinical and Topographic Anatomy. Morris-Jackson: Human Anatomy, 7th ed., Sec. 14, 1923, p. 1433.

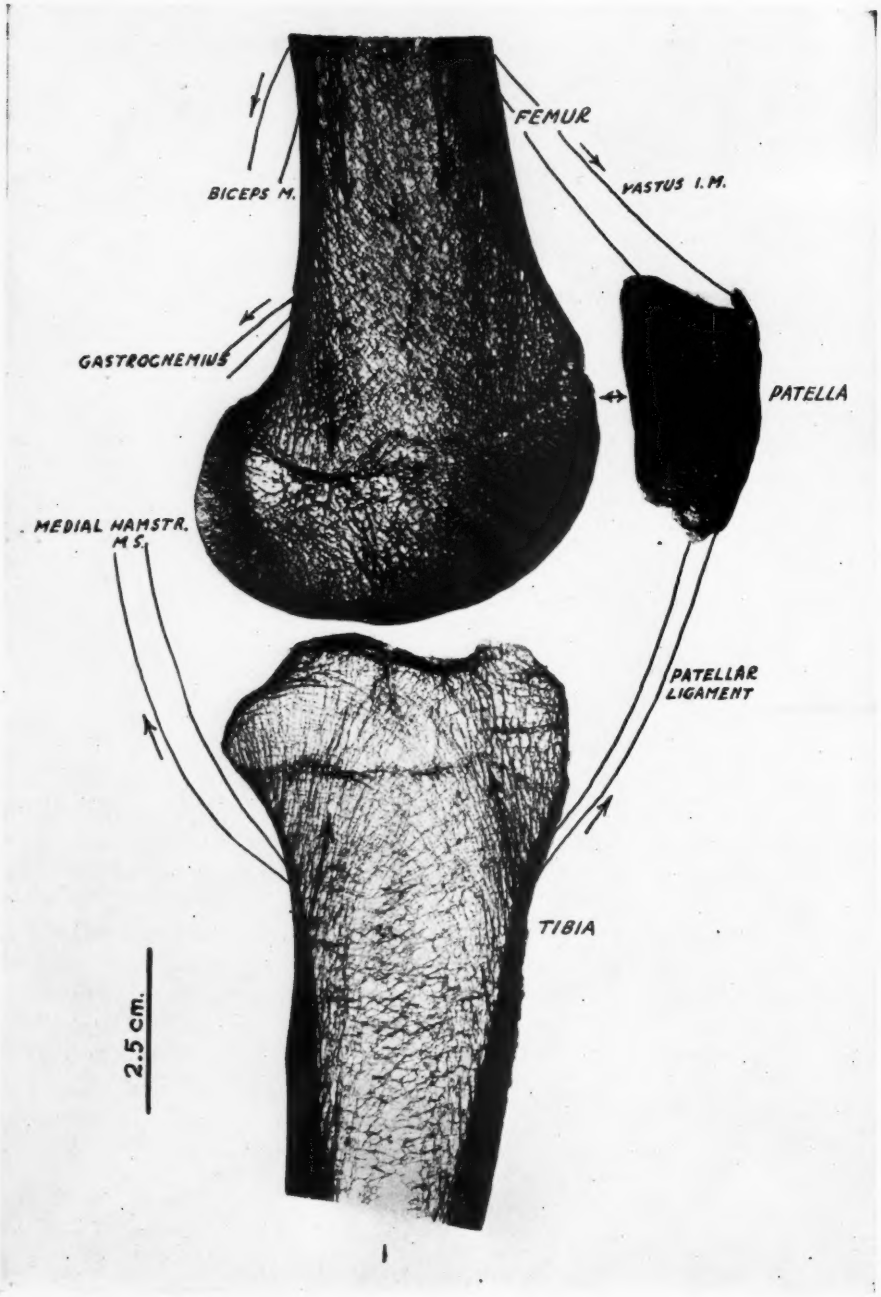

Plate I, Fig. 1. Roentgenogram of sagittal section of the human knee joint, femur, patella, and tibia. Natural size. In Fig. 1 the joint is represented in the extended position, whereas, in Figs. 2 and 3 there is progressive flexion. The point of contact of the femoral condyles with the tibia changes each moment, in the bent position the back of the femoral condyles being in contact with the tibia, in the extended position the lower part of these condyles being in contact with the tibia. In this action the pressure stresses

(Conclusion of legend of Plate I, on opposite page.)

radiate each time from a point situated more to the back. From each point of contact the stresses radiate upwards and backwards. These lines cross in many places, the spaces between the trabeculæ being small near the articular surface. The cancellous trabeculæ are arranged along the changing paths of the back-pressure vectors of the quadriceps extensor femoris muscle and the hamstrings and gastrocnemius muscles. The various transverse and oblique cancellous trabeculæ are produced by the variable directions of the back-pressure caused by the changing angle and direction of application of muscle forces during contraction in the production of joint range of motion.

These apparent splittings and crossings of the bony trabeculæ do not have a constant right angle or orthogonal relationship—some angles are acute and some obtuse. These variable crossings produced by the variable angles of application of muscle forces give a latticework appearance to the cancellous bone.

The dominant direction of the cancellous trabeculæ corresponds to the dominant action manifested at the particular joint. At the knee this dominant action is flexion and extension. The slight number of transversely directed trabeculæ that cross the dominant group of flexion and extension trabeculæ is due to the limited action of medial and lateral rotation at the knee joint. At the ankle medial and lateral rotation is more easily and powerfully executed, therefore trabeculæ transversely arranged are evident.

II. BRIEF HISTORICAL REVIEW OF THE ARCHITECTURAL SIGNIFICANCE OF CANCELLOUS BONE

Ward[7] and Wyman[8] compared the femoral neck to a derrick supporting a load; the stresses in the cable in the derrick are tensile and in the boom compressive.

Humphry[9] stated that the two groups of cancellous trabeculæ in the head and neck of the femur cross at right angles and are perpendicular to the articular surface at all points.

In 1866 H. von Meyer,[10] at the Zurich meeting of the "naturforschende Gesellschaft," demonstrated a frontal section of the proximal end of the femur, and Culmann, the founder of graphostatics, thought that the cancellous bone elements crossed at right angles like the directions of greatest tension and greatest pressure in the crane to form stress trajectories. The resemblance between the trajectories in Culmann's crane and the cancellous pattern in the femoral neck was considered as identical.

The trajectories in Culmann's crane cross at right angles, because in elastic bodies the directions of greatest tension and pressure cross at right angles.

Julius Wolff,[11] in his treatise on "The Law of the Transformation of Bones," confined his observations to the proximal extremity of the femur and emphasized what he considered the right angular crossings of cancellous bone which he called "orthogonality." Wolff states, "wheresoever stresses of pressure and tension are caused in a bone, be it by pressing forces or by pulling forces, formation of bone takes place."

W. Roux[12] also emphasized the equivalence of pressure and tension in bone formation and stated that the external form as well as the internal structure of bone is determined mechanically and mathematically by tension and pressure. He stated that the elements of cancellous bone coincide with the stress trajectories of graphostatics. The various parts of the skeleton were called "trajectorial structures."

Murk Jansen,[13] in an excellent exposition of this subject of trajectorial structure, points out that the theory stands or falls with the constancy of the angle at which

7Ward, F. O.: Outlines of Human Osteology. London, 1838.

8Wyman, Jefferies: On the Cancellated Structure of the Bones of the Human Body. Boston Jour. of Natural History, 1857, VI.

9Humphry, G. M.: A Treatise on the Skeleton. Cambridge, 1858.

10von Meyer, H.: Die Architectur der Spongiosa. Reichert und Dubois-Reymond's Archiv., 1867, p. 615. Statik und Mechanik des Menschlichen Knochengerüstes. Leipzig, 1873.

11Wolff, J.: Law of the Transformation of Bone, 1892, p. 88.

12Roux, W.: Beitrage zur Morphologie der functionellen Anpassung Beschreibung und Erlauterung einer knochernen Kniegelenkankylose. Archiv. f. Anatomie u. Entwickelungsgeschichte, 1885, p. 120.

13Jansen, Murk: On Bone Formation, 1920, pp. 13, 14, 16, and 56.

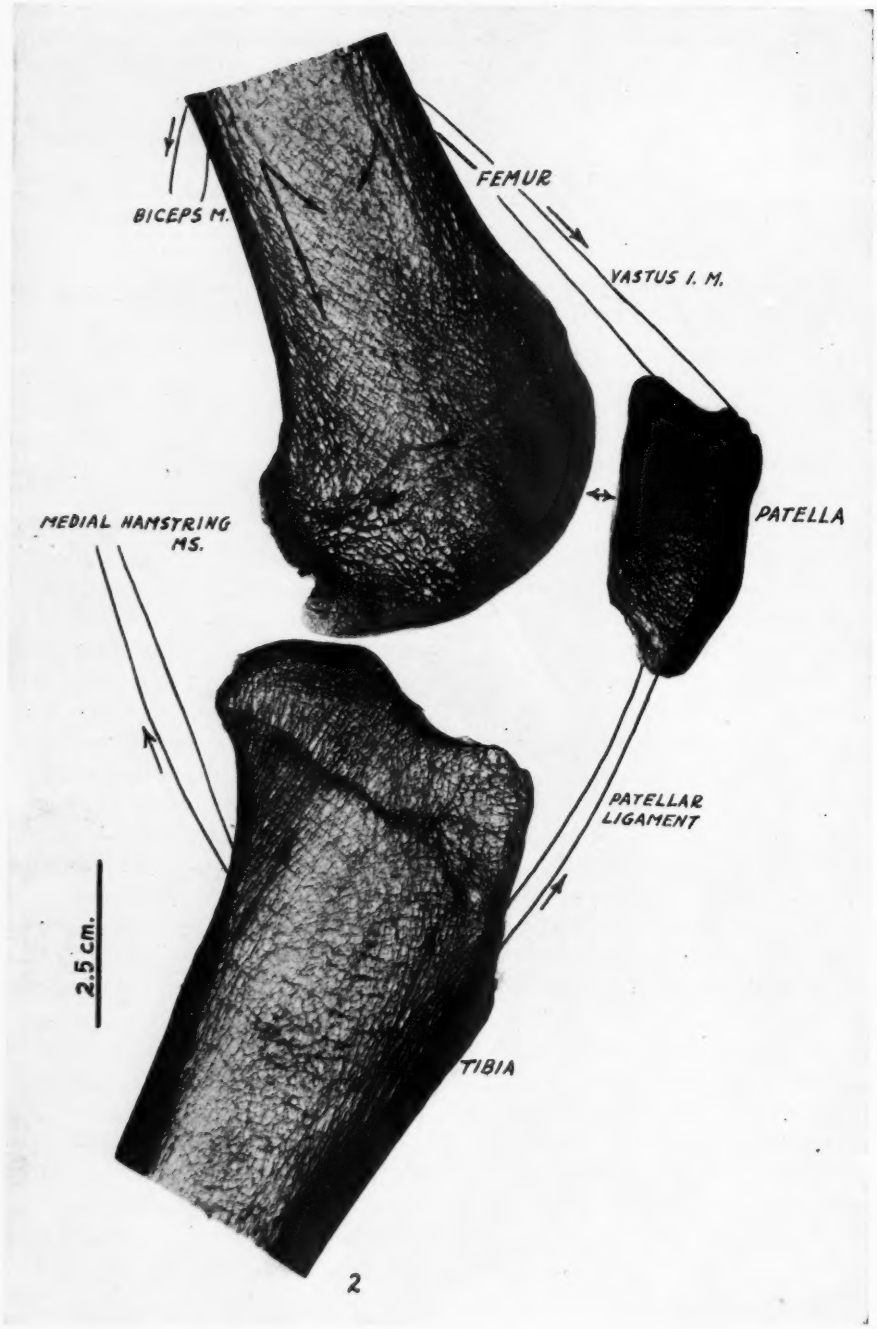

Plate II, Fig. 2. Roentgenogram of sagittal section of the human knee joint, femur, patella, and tibia. Natural size. Semi-flexed position. See explanation in Plate I, Fig. 1.

these elements cross, and that "the incorrectness of this denomination will be proved, when further inquiry shall show that the angles at which these elements cross, vary, *i.e.*, are sometimes right, sometimes acute and obtuse."

In brief, the Culmann-Meyer-Wolff-Roux dualistic doctrine of bone formation, dependent on both tension and pressure, is dependent on the supposed constant right angular crossings of the cancellous bone trabeculæ.

E. Zschokke,[14] B. Solger,[15] F. Bähr,[16] E. Albert,[17] K. Budinger,[18] as well as Murk Jansen,[13] have assailed the right angular crossing, or orthogonality, theory of cancellous bone. The idea of the equivalence of both tension and pressure, however, in bone formation is deeply rooted and is still taught.

John C. Koch,[19] in an excellent mathematical analysis of the femur, lays emphasis on the static pressure of body weight and practically ignores the dynamics of muscle action. He states: "Though it is recognized that the action of the muscle exerts an appreciable effect on the stresses in the femur, it is relatively small and very complex to analyze. For this reason the effect of the action of the muscles will not be investigated further in this study." He states that the muscles of the thigh could develop only one-seventh of the strength of the femur.

The writer agrees with Koch that the proportions of the femur have a definite mathematical relationship between the body weight and the internal structure of bone. Koch emphasizes the dead static weight of one hundred pounds on the femoral head which he uses in his analysis of the femur. The writer emphasizes the dynamic back-pressure of direct muscle action which normally varies with body weight and build. Koch stresses both tension and pressure in bone formation. The writer does not deny that bone resists tension but denies a rôle to tension on bone formation.

R. Thoma[20] has accepted the Culmann-Meyer-Wolff-Roux theory of the trajectorial structure of bone in analyzing the structure of the skull.

The compression of the skeletal colloids in the processes of differential growth and muscle function results in skeletal consolidation. This hardened tissue produced by pressure may transmit tension stresses as well as resist deformation due to compression. The formative, trophic stimulus, however, is pressure, not tension. Murk Jansen[13] has demonstrated in deformed bones that where pressure is eliminated and only tension remains the bone undergoes atrophy. On the other hand, where pressure is increased within an undetermined maximum the density of the bone increases. This pressure, furthermore, is remittent and not constant in nature. Zschokke stated that the remittent pressure of muscle action is often far greater than the static, and, therefore, must not be neglected in the explanation of the texture of cancellous bone.

Murk Jansen[13] quotes Christen as follows, in substantiation of the above assertion by Zschokke: "The correctness of this opinion may be illustrated by a simple example. In standing on one leg with the heel raised from the ground, the body weight is entirely transmitted to the ground through the metatarsal heads, and the latter are mutually pressed with the same force, *f.i.*, 60

14Zschokke, E.: Weitere Untersuchungen über das Verhältniss der Knochenbildung zur Statik und Mechanik des Vertebraten-Skelettes, Zurich, 1892.

15Solger, B.: Der gegenwartige Stand der Lehre von der Knochen-Architectur, Moleschott, 1899, XVI.

16Bähr, F.: Betrachtungen über die statischen Beziehungen des Beckens zur unteren Extremitat. Deutsche Ztschr. f. orth. Chir., 1899, V, 55.

17Albert, E.: Einfuhrung in das Stadium der Architektur der Rohrenknochen. Holder, Wien, 1920. Die Architektur der Tibia. Wien. med. Wchnschr., 1920, Nos. 4, 5, 6.

18Budinger, K.: Der Spongiosabau der oberen Extremitat. Ztschr. f. Heilkunde, 1903, XXIV (n. f. IV).

19Koch, John C.: Laws of Bone Architecture. Am. Jour. Anatomy, 1917, XXI, 224.

20Thoma, R.: Ein Beitrag zur Histomechanik des Skelettes u. zur Lehre von dem interstitiellen Knochenwachstum. Virchow's Archiv., 1907, CLXXXVIII, 303.

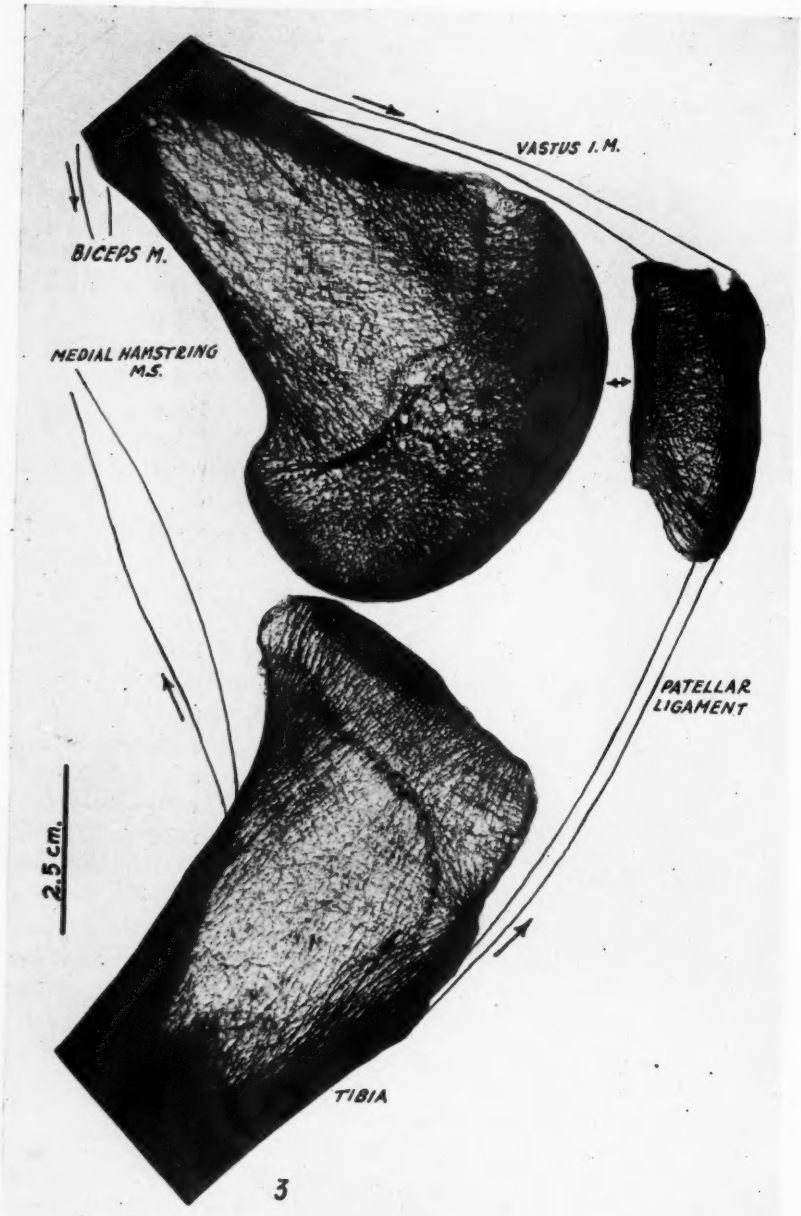

Plate III, Fig. 3. Roentgenogram of sagittal section of the human knee joint, femur, patella, and tibia. Natural size. Flexed position. The muscle forces acting on the knee joint are represented in outline. The back-pressure vectors produced by these muscles are represented by arrows within the bone structure. The direction of these arrows representing the back-pressure vectors of muscle action change with every possible position of joint range in mobilization. The dense cancellous structure produced by the articulation of the patella and femur is definitely evident.

There is a characteristic architecture of the cancellous bone in the ventro-dorsal plane at the lower

(Conclusion of legend of Plate III, on opposite page.)

end of the femur, which represents the type of rotation structure observed in the convex side of monaxial joints. On the concave side of monaxial joints the cancellous trabeculæ are likewise arranged to coincide with the stresses of back-pressure vectors produced by muscle action. In the upper part of the tibia the pressure acts on about the same point in the various positions of flexion. There are, therefore, a smaller number of trabeculæ and fewer crossings than in the lower end of the femur. The spaces between the bony trabeculæ are, therefore, larger on the concave side of monaxial joints, but the bone trabeculæ themselves are laid down along the paths of the chief pressure stresses produced by muscle action. There is a dominant convergence of the pressure stresses on the convex side and divergence of these stresses on the concave side of monaxial joints. There is a predilection for the typical architecture of the cancellous bone in the direction of flexion and extension. The direction of the dominant cancellous trabeculæ on the convex side of the joint resembles the convergent refraction of light rays to a focal point passing through a convex lens; on the concave side of the joint they resemble the divergent refraction of light rays passing through a concave lens. There are, however, other directions of cancellous bone than that of the dominant joint action due to subdominant actions executed at the joint. These actions form the cross-bars that form variable angles with the dominant flexor-extensor system of cancellous trabeculæ.

Kg. This, too, is approximately the force with which the body weight presses the tibia on the arch of the foot. Now the quadriceps in order to maintain the tip-toe position has to balance the pressure against the metatarsal heads. This muscle acts with respect to the turning axis of the foot joint on a lever arm three times as short as does the pressure of the ground against the metatarsal heads. It must, therefore, develop a force which is three times as great, *i.e.*, transmit a pressure thrice as great through the skeletal parts situated between its points of origin and insertion. Hence the tibia has to bear a pressure of $60 + 3 \times 60 = 240$ kg."

Solger[15] states that the basis of the facts on which to found a new theory of the bone elements is not nearly wide and deep enough. Murk Jansen[13] made an excellent start by attributing to muscle action the structure of cancellous bone.

The writer in this paper presents additional evidence that apparently points to the back-pressure vectors produced by muscle pull, mobilizing monaxial, biaxial, and triaxial joints as the dominant cause of the pattern of cancellous bone. In the actions of balanced antagonistic muscle groups maintaining the erect posture, back-pressure is more nearly parallel to the long axis of the bones. This is the attitude of dominant extension action. During flexion, back-pressure paths are produced that deviate progressively from the long axis in a more oblique direction. During medial and lateral rotation back-pressure vectors are produced in the skeleton that are in a more nearly parallel path to the articular surface and at right angles to the long axis of the bone. In addition, there is produced back-pressure by the tension of the capsular and other ligaments as well as the periosteal limiting membrane. Along all variable active and passive paths of back-pressure, bone is produced as a structural expression of internal stresses that resist the tendency to deformation caused by the changing direction of the external forces during joint mobilization by muscle action.

III. WHAT IS A VECTOR?

It is a quantity or magnitude that has direction, such as stress and strain, lines of force, flow of heat and fluid, electricity. All of these involve two parts, *i.e.*, magnitude and direction. All such quantities are vector quantities. Cancellous bone is the objective structural expression of vector quantities which are the back-pressure resultants of group muscles in alternate action. These trabeculæ of cancellous bone are not due to the static pressure of body weight in the upright posture, but are directly arranged along the changing lines of the back-pressure

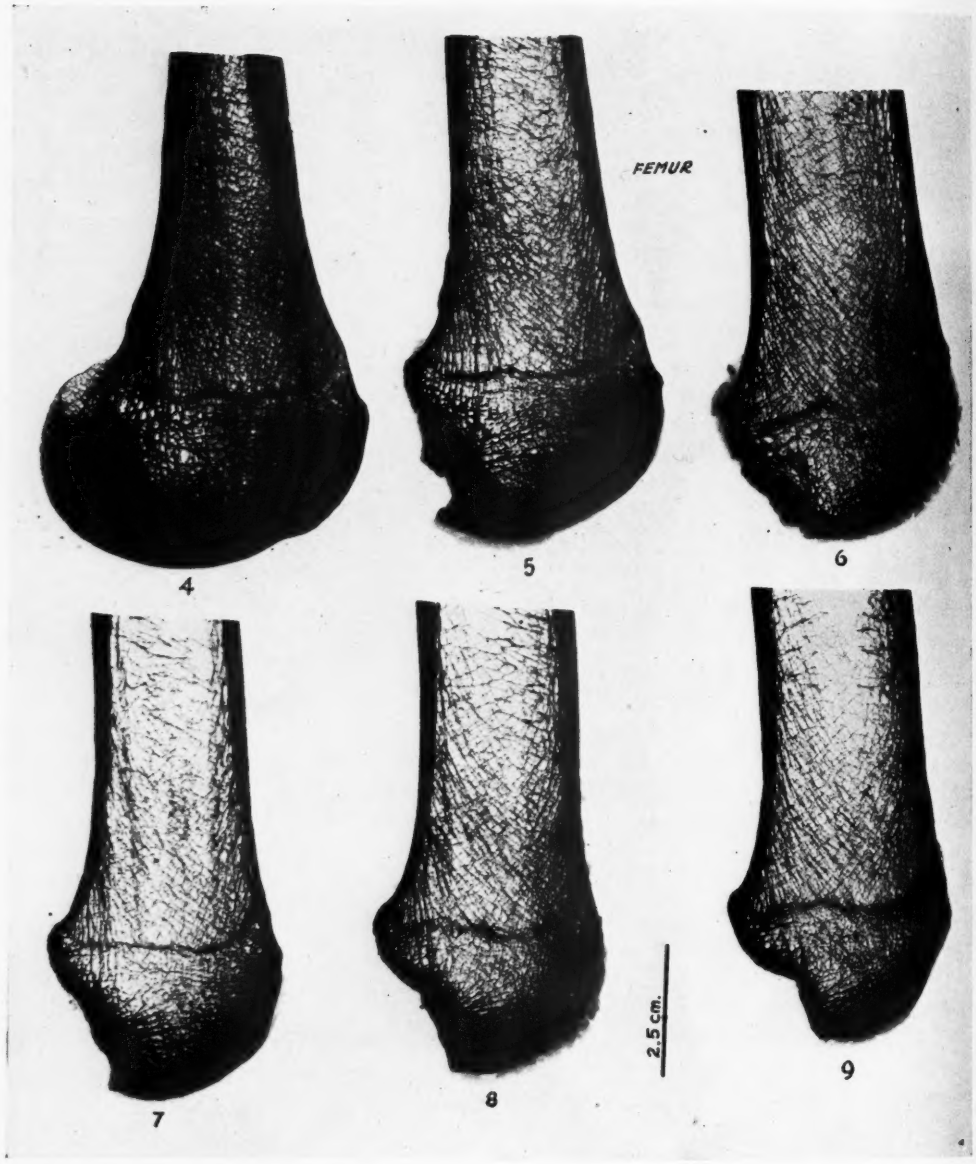

Plate IV, Figs. 4 to 9. Roentgenograms of sagittal sections of the lower end of the femur. One-fifth reduced. The variable architecture of the cancellous bone of the lower end of the femur in a sagittal plane through the center of the lateral condyle (Fig. 4) to the mid-sagittal plane (Fig. 9) through the intercondyloid fossa is illustrated. The inverted Gothic arches irregularly placed are produced by the back-pressure vectors of the extensor and flexor muscles of the knee joint. The dense cancellous bone produced at the condylar articular surface and the trochlear surface of the patella is in contrast to the inverted Gothic architecture farther away from the articular surfaces.

The ventro-dorsal arrangement of the cancellous bone trabeculæ in the lower extremity of the femur, with the variable crossings of the bone trabeculæ at right, obtuse, and acute angles, represents the characteristic type of rotation structure on the convex side of monaxial joints.

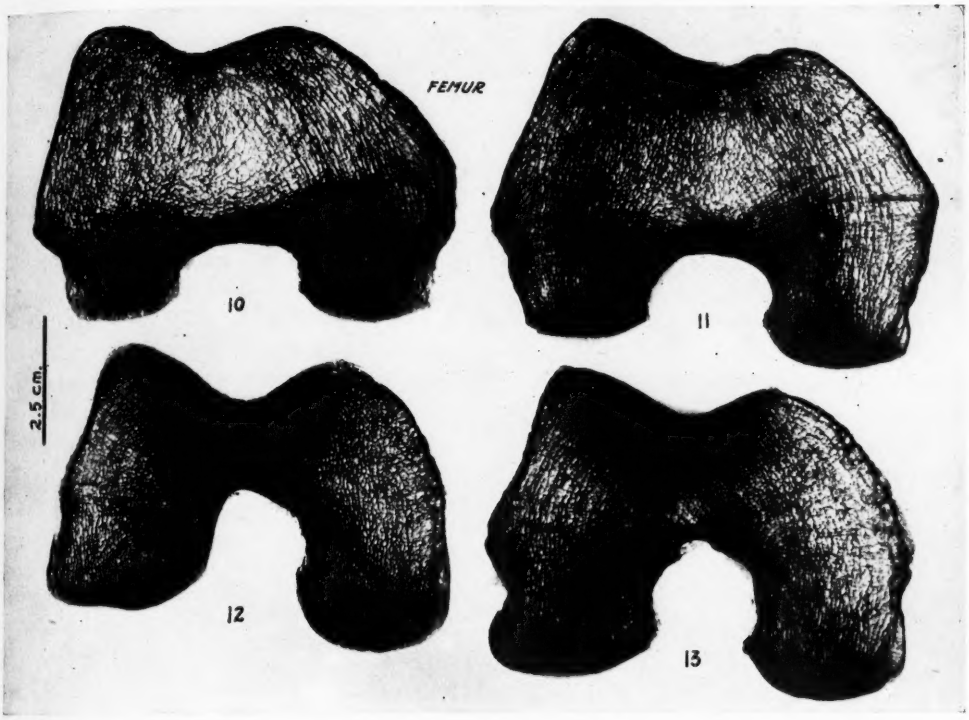

Plate V, Figs. 10 to 13. Roentgenograms of cross-sections of the lower extremity of the femur. One-fifth reduced. There is a series of diverging bone trabeculæ radiating from the intercondyloid fossa in the lower end of the femur. These are produced by the back-pressure of the crucial ligaments in alternate traction, during flexion and extension of the knee joint. Albert (1900) calls these the "radiant" trabeculæ, but he adds: "What mechanical meaning this texture may have, will have to be found by later research" (page 48; see Footnote 17 for citation).

due to muscle action and impact of the joint surfaces, in mobilization, in any position. The back-pressures of reciprocal and antagonistic groups of muscles in alternate traction and contraction are found as the resultants of muscle forces by means of the parallelogram of forces. It is the mutual functional interaction between the muscles and skeleton that sustains body weight in the upright position and body posture. Body weight is not conducted as a dead load directly from bone to bone, but indirectly through the dynamic activity of the musculature that by means of intensity of muscle pull determines the magnitude and direction of the back-pressure vectors which are crystallized out as the cancellous bone trabeculæ where the volume of the skeleton is increased at the extremities of long bones and in short bones.

IV. THE OBJECTIVE EVIDENCE

The back-pressure vectors of muscle action determine the structure of cancellous bone in the human knee and ankle monaxial joints

The dominant direction characterizing the pattern of the cancellous architecture in the human knee and ankle monaxial joints is in that of flexion and extension. These two actions are the dominant ones manifested at the knee and ankle joints. Corresponding to the back-pressure vectors in the skeleton

of the acting flexor and extensor group of muscles, there are found cancellous trabeculæ typically arranged to resist or conduct this back-pressure. At the knee there is limited medial and lateral rotation. At the ankle there are the dominant actions of flexion and extension and subdominant ones of inversion and eversion, medial and lateral rotation. There will be found, therefore, back-pressure vectors objectively evident as cancellous bone trabeculæ that cross the dominant trabeculæ of flexion-extension, at variable angles, depending on the position of the bones in joint range of motion.

The intersections are not all right angular or orthogonal by any means; some are acute, some obtuse. Inspection of these intersections in the roentgenograms (Plates I to VIII) is convincing on this point, a fact which was also observed by Murk Jansen.[13] The observer should study the roentgenograms as well as the context of the legend with each roentgenogram.

There is a characteristic architecture of the cancellous bone in the ventro-dorsal plane at the lower end of the femur which represents the type of rotation structure observed in the bone of the convex side of monaxial joints. The pressure point of contact of the convex component of a monaxial joint changes each moment in passing from an extended position to one of flexion, or *vice versa*. In this action each bone carries active back-pressure of muscle action toward the articulating surface and reactive pressure of contact in the reverse direction produced by the opposed joint companion. The cancellous bone is arranged along the changing paths of back-pressure in the changing position of the bones by muscle action. Where the pressure converges and the paths are close together the bone is found to be densest, resembling an irregular hub of a sphere with converging spokes.

On the concave side of monaxial joints the cancellous trabeculæ are likewise arranged to coincide with the internal stresses of back-pressure vectors of muscle action. In the upper part of the tibia the pressure acts on about the same points in the various positions of flexion. There are, therefore, a smaller number of trabeculæ with fewer crossings than found in the convex condylar articulation of the femur. The spaces between the trabeculæ in the upper end of the tibia are larger on the concave side.

There is a dominant convergence of the pressure stresses with many intersections of right, obtuse, and acute angles (Plates I to VIII) of the corresponding trabeculæ on the convex side, and divergence of these stresses and corresponding trabeculæ on the concave side of monaxial joints. There is a predilection for the trabeculæ to be placed in a typical manner to resist the pressures of flexion and extension muscular activities. On the convex side the trabeculæ converge from the articular aspect of the epiphyseal end toward the diaphysis of the same and opposite sides, corresponding, respectively, to extension and flexion, as well as with other accessory limited actions. The paths of these latter actions cross the dominant flexor-extensor paths at right or obtuse angles, forming the more transverse bars in the apparent latticework of the cancellous bone.

The back-pressure vectors are crystallized as bony trabeculæ and are arranged on the convex and concave sides of monaxial joints somewhat like the light rays refracted through a convex and concave crystal lens. On the convex side there is a tendency for the main groups of trabeculæ to converge to a focal point of maximal pressure, whereas, on the concave side, the bone trabeculæ diverge. This picture is confused, however, by other trabeculæ of bone produced by the subdominant actions at the joint, as well as by the compression action of the tense capsular and crucial ligaments in joint motion. The compression action of the periosteal

limiting membrane at right angles to its line of longitudinal traction may not be ignored in the formation of some of the transverse and oblique bars of bone near the metaphysis and diaphysis. The compression action between the epiphyseal and diaphyseal

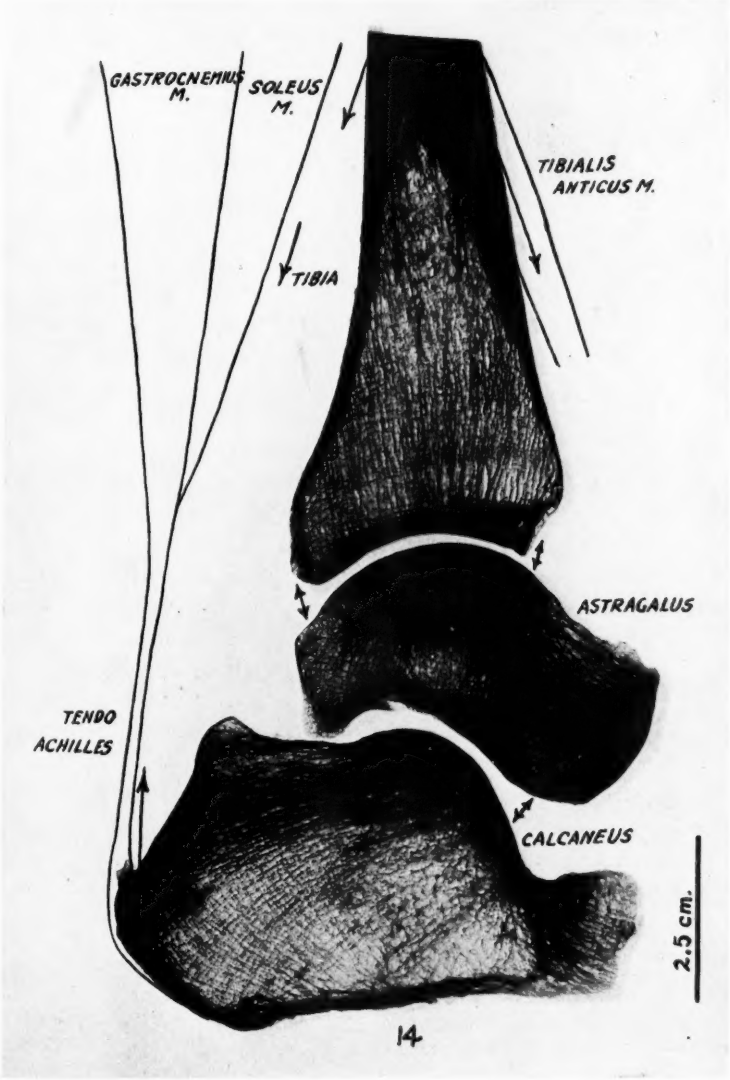

Plate VI, Fig. 14. Roentgenogram of mid-sagittal section of the human ankle joint, caudal end of tibia, astragalus, and calcaneus. Natural size. On the convex aspect of the astragalus there is a convergence of cancellous trabeculæ, whereas, on the concave tibial aspect of the ankle joint there is a divergence of the bony trabeculæ. These trabeculæ are arranged along the chief planes of action of flexion and extension at the ankle joint. The oblique and more transversely directed bony trabeculæ are related to the actions of inversion and eversion as well as medial and lateral rotation.

The arrows representing the back-pressure vectors of muscle action, placed within the bone, change their positions with the changing degrees of muscle action and position of the foot. In Figs. 15 and 16 there is a progressive change in the relationship of the bones to the position of marked hyperextension in the foot.

growth zones resulting in transverse plates of metaphyseal bone during periods of heightened growth and muscle activity may not be omitted as the cause of certain transverse bars of bone previously known as "lines of arrested growth."

V. THE BACK-PRESSURE VECTORS OF MUSCLE ACTION DETERMINE THE STRUCTURE OF CANCELLOUS BONE IN THE HUMAN BIAXIAL METATARSO-PHALANGEAL JOINT OF THE GREAT TOE.

The great toe is capable of strong flexion and extension, but weaker adduction and abduction actions. There is limited action between the above two chief planes of action. By inspection of Plates IX and X it is evident that there is greater confluence and density of the cancellous trabeculæ in the head of the first metatarsal (Fig. 18), in the sagittal plane of flexion and extension, than in the head of the first metatarsal (Fig. 20), cut in a plane at right angles to the sagittal plane or parallel to the plantar surface. The section of the head of the first metatarsal (Fig. 22) is in the plane of action of abduction and adduction. These actions are weaker than flexion and extension and consequently the cancellous bone that resists abduction and adduction (Fig. 20) is looser in texture than that which resists flexion and extension (Fig. 20).

The cancellous bone is, likewise, disposed in all possible directions between the two chief planes of action of the biaxial metatarso-phalangeal joint. The greater density with more numerous intersections at variable angles of the cancellous bone is laid down in the plane of the more forcible actions of flexion-extension than in that of abduction and adduction. This characteristic is also noted at the caudal extremity of the radius, in which the plates of cancellous bone are denser in the plane of flexion and extension than in that of abduction and adduction.

With an increasing number of planes of action executed at a joint such as in the triaxial diarthrodial hip and shoulder joints, there is a still greater increase of cancellous bone trabeculæ corresponding to each actual plane of action.

VI. THE BACK-PRESSURE VECTORS OF MUSCLE ACTION DETERMINE THE STRUCTURE OF CANCELLOUS BONE IN THE HUMAN TRIAXIAL HIP JOINT.

In the monaxial knee joint the cancellous trabeculæ have a definite arrangement corresponding to the plane of flexion and extension. In a biaxial joint, *i.e.*, the metatarso-phalangeal, the typical monaxial rotation type of structure is broken up where the movements occur in multiple planes between flexion-extension and adduction-abduction.

The diarthrodial hip joint has capacity for movement between all the three planes, *i.e.*, sagittal, coronal, and transverse, as well as a combination through these planes executed in circumduction. The femoral head in a slightly oblique transverse section to the long axis of the neck (Plates XI and XII) has a homogeneous spongy structure. The elements start from the articular surface relatively equal in all directions, and cross at equal distances, leaving fairly equal spaces between the cancellous trabeculæ except in the middle of the head. There is an apparent oblong convergence to a focal zone at the middle of the head. The bone elements, therefore, in the head of the femur are disposed in the direction of the back-pressure of the multiple muscle forces.

The trabeculæ start from the articular surface, meet in the middle, and pass to the cortical bone of the opposite side in coronal sections (Plates XV, XVI, and XVII). The more dense medial group of trabeculæ that extend more directly cephalad from the cortical bone on the medial aspect of the diaphysis and metaphysis and concave side of

the neck, are definitely related with the actions of adduction and flexion. The less dense group of trabeculæ that have a parabolic arched disposition on the convex side of the femoral neck, and extend from the trochanter major and lateral aspect of the cortical bone of the diaphysis and metaphysis, are definitely related with extension and abduction actions at the hip joint.

On the convex side of the femoral neck,

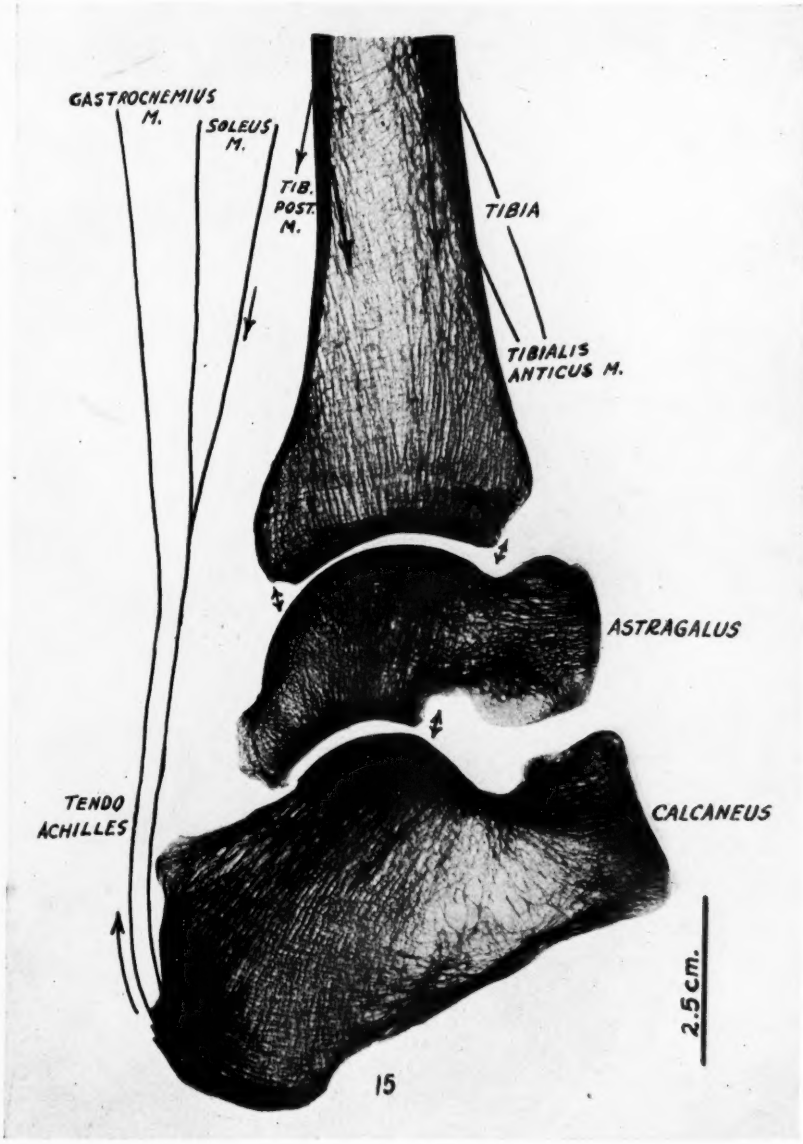

Plate VII, Fig. 15. Roentgenogram of mid-sagittal section of the human ankle joint, caudal end of tibia, astragalus, and calcaneus. Natural size. The astragalus and calcaneus are placed in the position of mid-extension of the foot.

therefore, there are back-pressure vectors due to the muscle pull of the glutei from the lateral aspect of the trochanter major and the obturator muscles, pyriformis and gemelli from the medial side of the great trochanter. The dynamic force of the muscles acting on the hip may exceed the static pressure of body weight. Because the

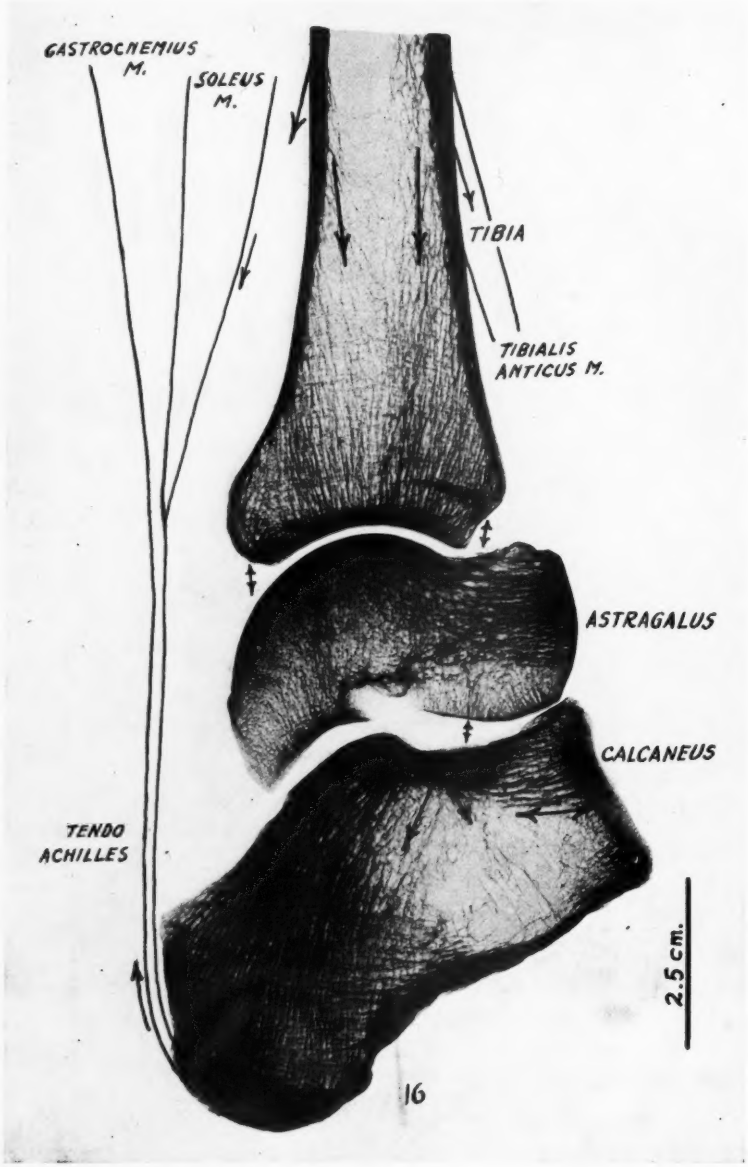

Plate VIII, Fig. 16. Roentgenogram of mid-sagittal section of the human ankle joint, caudal end of tibia, astragalus, and calcaneus. Natural size. The astragalus and calcaneus are placed in the position of hyperextension of the foot.

femoral neck is bent, supposedly by body weight but in reality by muscle pull (See developing cow's femur, with marked epiphyseal development and markedly bent neck before birth, Plate XXI), the curved lines on the convex aspect of the femur have been interpreted as caused by tension action of the pure static weight of the body in the erect attitude.

That these elements are so disposed that they could resist a bending or tensional stress is not denied, but they represent a crystallized structural expression of the back-pressure vectors of muscles acting toward the articular surface of the femur from its cephalo-lateral aspect, *i.e.*, trochanter major and lateral aspect of the cortex of the diaphysis and metaphysis.

The observer should note the angles of intersection made by the more straight group of adductor-flexor trabeculæ on the concave side of the neck with those on the convex side, which are the abductor-extensor group of cancellous trabeculæ. There will be found right, acute, and obtuse angles of intersection. A supposed constant right angular or orthogonal intersection is by no means a constant finding and in many sections is the least dominant angular type of intersection. The planes of sections illustrated have been accurately cut with an electric band saw; the fat removed by boiling in 2 per cent sodium hydroxide for from one week to ten days for from four to eight hours a day; the sections then bleached in hydrogen peroxide before roentgenograms are taken at a 42-inch target distance, films in exposure holders, 50 kilowatts and 10 milliamperes current, 5–10 radiator tube.

The femoral neck is not a typical trajectorial structure. The trabeculæ on the convex side of the femoral neck are neither stimulated into actuality nor maintained by tension stresses. These elements do not correspond with the direction of greatest tension but do correspond to the mathematical stress diagram of back-pressure vectors of muscle pull that changes in direction at its point of application each moment during the mobilization of the hip joint. The trajectorial structure implies constancy of angles of crossing and the inconstancy of these angles points to a more biological and dynamic concept of muscle action in establishing and maintaining the internal pattern of the cancellous trabeculæ of bone.

The calcar femoral or femoral spur of Merkel (Plates XIII and XIV) is one of the classical examples of a condensed group of back-pressure vectors produced primarily by the two powerful antagonistic muscles in action, namely, the flexor, ileo-psoas and the extensor of the hip, the gluteus maximus. No attempt at explanation of this structure on the basis of dynamics has hitherto been presented. The ileo-psoas is inserted on and below the lesser trochanter, whereas the bony insertion of the gluteus maximus is on the third trochanter or gluteal tuberosity.

According to Dean Lewis[6]: "The strong process, femoral spur or calcar (Merkel), which, arising from the compact tissue on the medial and under side of the neck, just above the lesser trochanter, spreads laterally towards the trochanteric (digital) fossa, also affords strength, and its degeneration probably plays an important part in the fractures of the neck."

The femoral spur is placed in the line through which the weight of the body falls, and adds to the stability of the neck, but the immobile static load of body weight is not the direct producer of this spur. The calcar femorale is caused by the condensed converging group of back-pressure vectors of the hip-flexor, ileo-psoas and the hip-extensor gluteus maximus, the two main balanced muscles, in addition to others, that directly sustain body weight, in the upright posture, by their osseous attachments. The calcar femorale becomes markedly atten-

uated in old age and in those individuals who have been bedridden for a long period of time, due to the lack of normal use of the hip-flexor, the ileo-psoas, and the hip-extensor, the gluteus maximus muscles.

The load of body weight is not trans-

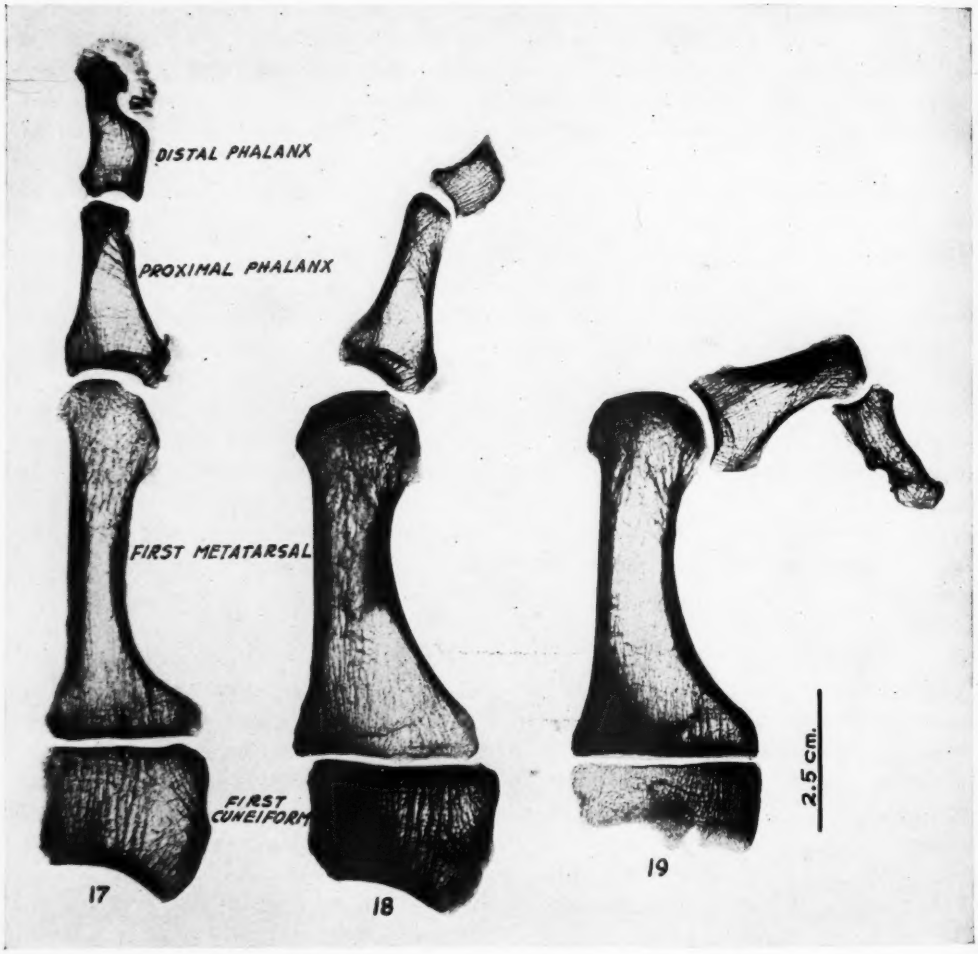

Plate IX, Figs. 17, 18, and 19. Roentgenograms of mid-sagittal sections (dorso-plantar) through the axis of the first metatarsal bone of the left foot. One-fifth reduced. In the plate from below upwards are represented the first cuneiform, metatarsal, proximal and distal phalanges of the hallux. From Figs. 17 to 19 the phalangeal bones are placed in positions of advancing degrees of flexion. There is a greater tendency for the cancellous bone structure to form a confluence in the sagittal plane or in the direction of flexion and extension. At the metatarso-phalangeal joint, however, the great toe is capable of executing the movements of limited adduction and abduction. This type of joint, therefore, is a biaxial articulation and has the cancellous lamellæ arranged between the planes of flexion-extension and adduction-abduction, the bone being most dense in the plane of dominant activity. In Plate X, Fig. 20, the first cuneiform, first metatarsal, proximal and distal phalanges of the hallux are cut at right angles to those illustrated in Plate IX. The plane of section is parallel, therefore, to the sole of the foot. The greater density of the cancellous tissue in the head of the first metatarsal in Fig. 18 should be compared with the more loose cancellous structure in the head of the first metatarsal in Fig. 20. It is evident that the sagittal system of cancellous bone is denser than that in the plane parallel to the sole of the foot, because the dominant actions of flexion and extension by far outweigh those of adduction and abduction. In this biaxial joint, therefore, there is a definite relationship between the density of cancellous bone and the course of the back-pressure stresses produced by muscle action.

mitted directly to the skeleton as a dead static load, but indirectly through the back-pressure action of the attached musculature. The normal body posture is the resultant of a reciprocal dependency and mutual interaction of normal nervous impulses and muscular tonicity on one side of the balanced reaction, and normal sufficiency and density of the skeleton on the other, in the neuromuscular and skeletal equilibrium. As stated previously, the dynamic force of the muscles acting upon the skeleton may exceed the static dead load of body weight.

The femoral neck is bent by muscle action during pre-natal life and the degree of curvature is directly proportional to the degree of muscular development. This fact is most strikingly exemplified in those animals that begin to walk as soon as they are born, especially the ungulates, *i.e.*, cow, horse, and deer. The degree of curvature in the neck and the advanced degree of epiphyseal bone development at the time of birth in the cow, for example, corresponds to that in the human of 12 to 15 years of age. As may be seen by a study of Plate XXI there is a marked correlation in advanced neuromuscular development corresponding with that of the skeleton. This is not a mere parallelism, as has been proved by the writer not only by morphological evidence but by experimental evidence under control conditions as well.

The cancellous trabeculæ on the convex and concave aspects on the bent femoral neck cannot be considered as simple units, for those on each aspect are composed of groups of bone that correspond to specific muscles and muscle groups in action. On the convex aspect the abductors, extensors, and external rotators are intermingled; on the concave aspect the adductors, flexors, and internal rotators form an intersecting group of trabeculæ. If specific muscles be eliminated from action by surgical excision, there will be a progressive corresponding disappearance of the cancellous bone that was actuated into structural expression by the back-pressure of these specific muscles in action. This is proved by the evidence presented in Plate XIX. The quadriceps extensor femoris muscle, patella, and patellar ligament were excised in a dog. The muscle was excised one inch cephalad to the patella. There was progressive atrophy of the anterior group of trabeculæ, produced by extensor action at the caudal end of the femur and proximal end of the tibia.

In studying the structure of the femoral neck in coxa vara, Jansen[13] states the following: "In short, the width of the elements on the concave and convex sides in the various femoral necks shows a parallelism with the degree of pressure stresses, whereas in the degree of tension stresses and the width of the bone elements any parallelism is wanting." He found, in coxa vara, the width of the bone on the concave side to be thickened, where the pressure is increased, and on the convex side thinned out, where the pressure is decreased and the tension increased.

Meyer[10] considered the transverse bone elements running parallel to and near the surface of the joint to be tension elements, the best examples being, at the lower end of the tibia, the bases of the metatarsal bones, the cuneiform and navicular; at the upper end of the tibia; the lower end of the femur, and the non-articular aspect of the patella. Some of these lines during the period of growth are formed by growth-additions to the shaft farther away from the articulations. These represent plates produced by increased pressure of heightened activity during growth.

Those transverse lines confined to the epiphysis close to the articulating surface are produced by the more transverse back-pressure vectors of the medial and lateral rotator muscles at the specific joints. The back-pressure of tension of stretched capsular ligaments will be resisted by cancellous

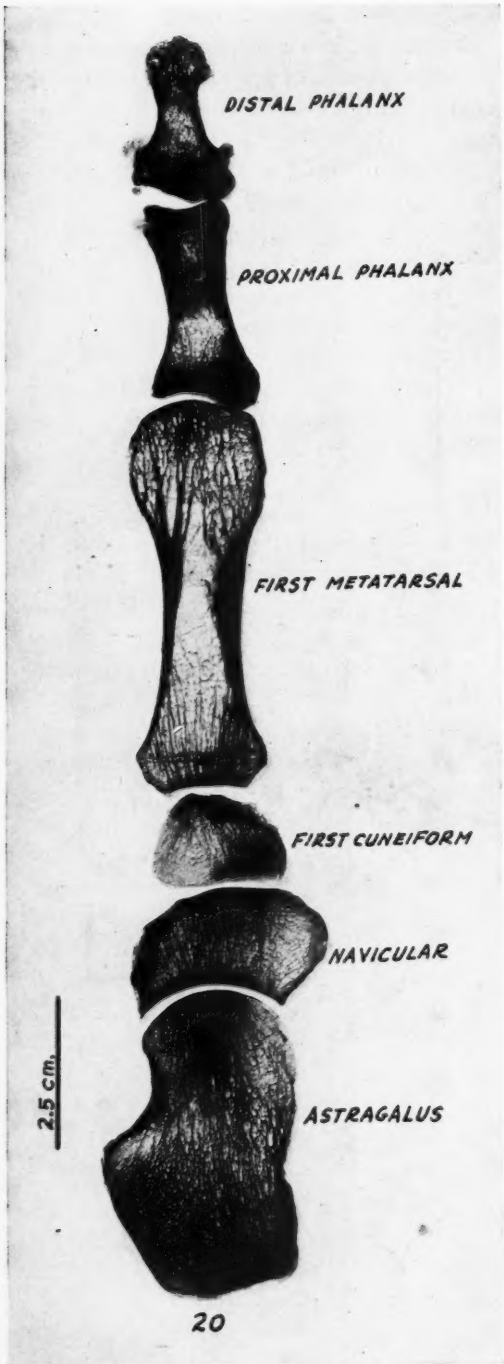

Plate X, Fig. 20. Roentgenograms of the bones of the left foot in the axis of the first metatarsal bone at right angles to the midsagittal plane. In other words, the sections of these bones are parallel to the sole of the foot (talus, navicular, first cuneiform, first metatarsal, proximal and distal phalanges of the hallux). One-sixth reduced.

(Conclusion of legend of Plate X.)

The observer should compare this plane of section of the biaxial metatarso-phalangeal joint with that taken at right angles to this plane, described in Plate IX, Figs. 17 to 19. At the metatarso-phalangeal, joint movements are carried out in the direction between the two planes of flexion-extension and adduction-abduction. The cancellous bone elements, therefore, are disposed in all possible directions between these two chief planes of action of the biaxial metatarso-phalangeal joint. The greater density of the cancellous bone is laid down in the plane of the more forcible movements, flexion and extension. This characteristic is also noted at the caudal extremity of the radius, in which the plates of cancellous bone are densest in the plane of flexion and extension action. With an increasing number of planes of action executed at a joint, such as in the triaxial joints of the hip and shoulder, there is a still greater tendency for the cancellous bone to be disposed along the back-pressure paths of muscle action in all of the possible positions of the mutual joint surfaces.

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bone more transversely directed than the main bone groups, whose axes are more nearly parallel to the long axis of the bone. The back-pressure produced by the stretched periosteum will be directed more transverse than parallel to the long axis of the bone, and will be resisted by transversely directed bone elements. The transverse as well as more longitudinally directed cancellous trabeculæ resist pressure in the path along which they are built, back-pressure being produced by variable actions of the muscle groups and by the back-pressure of the tension of ligaments and periosteum.

DISCUSSION

What is the osteoblast?—The writer does not intend to present the experimental evidence, at this time, in support of the answers to the following questions. This will be reserved for a future communication. The purpose of opening these questions at this time is to show the bearing of the study presented in this paper to the entire question of normal and abnormal bone growth

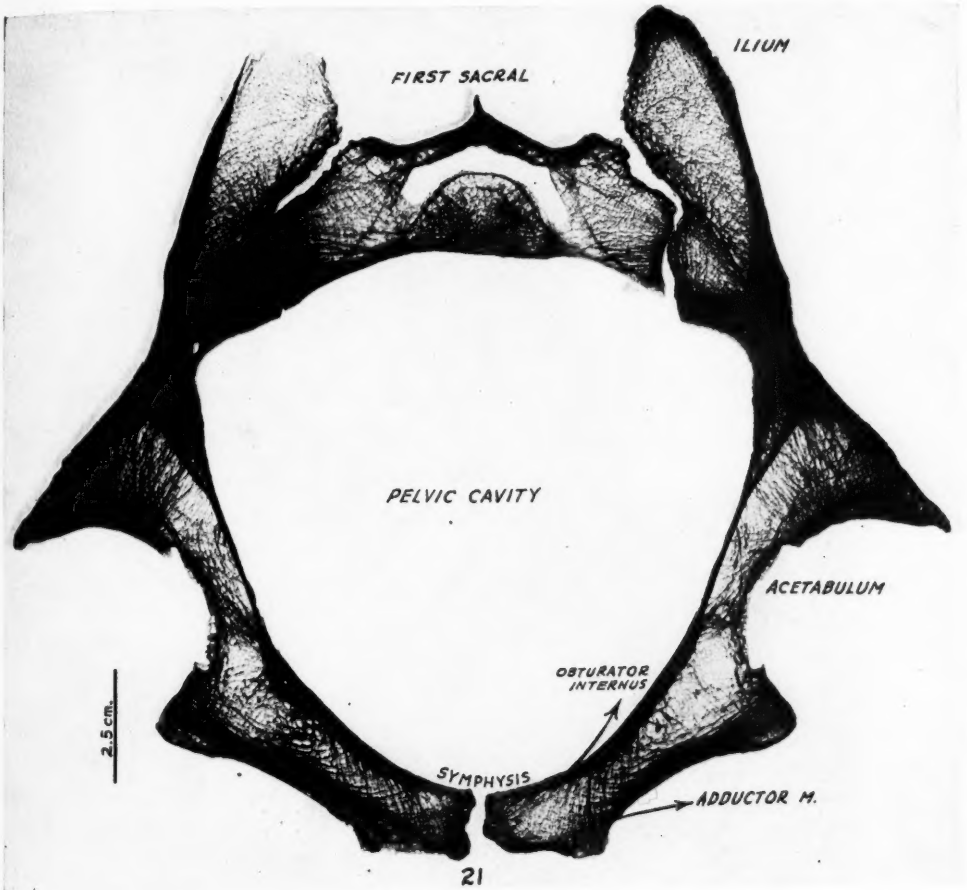

Plate XI, Fig. 21. Roentgenogram, oblique transverse section through the human pelvis. Two-fifths reduced. Note the diverging radiating trabeculæ of cancellous bone from the acetabular articular surface. The oblique and transverse elements correspond with the pressure stresses produced by the actions of adduction-abduction and internal and external rotation. Lateral to the symphysis pubis the pubic bone possesses a typical crucial structure of cancellous trabeculæ arranged along parabolic lines resembling superimposed Gothic arches. This same structure is found in the ilium, best seen in Plate XII, Fig. 22.

and maintenance. The biophysical aspect is as important as the biochemical one in the problem of bone origin. The biophysical conditions determine the site or localization of calcium deposition in both calcification and ossification. The resultant local chemical changes are consequences of an antecedent physical condensation of tissue by compression. The correlation of these physical and chemical factors when thoroughly known will answer the question of Sir Arthur Keith,[21] "Quid dicam de ossificatione?" But the problem of ossification will remain an enigma so long as the physical or chemical conditions of the problem are studied as isolated entities.

(a) What is bone?—Bone is a vascularized (organized) tissue adequately consolidated by the reaction of growing cells to an adequate compression stimulus: bone growth

[21] Keith, Sir Arthur: The Origin of Bone. Proc. Roy. Soc. Med., 1927, XXI, 301.

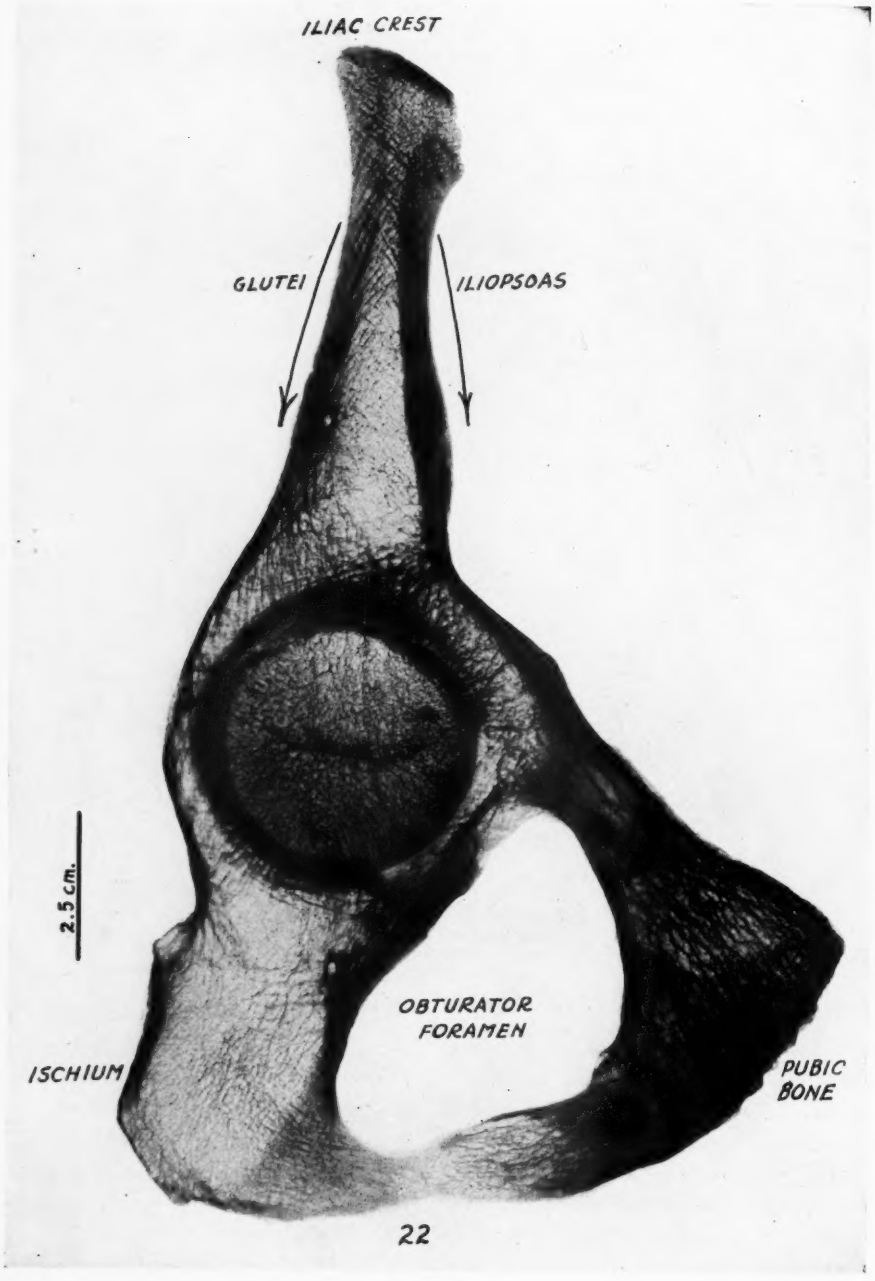

Plate XII, Fig. 22. Roentgenogram, an oblique sagittal section through the ilium, ischium, pubis, acetabulum, including this plane of section through the head of the femur, which is transverse to the long axis of the neck of the femur. One-fifth reduced. In this plane of section the femoral head has a spongy homogeneous structure. There is a coronal radiation of the cancellous bone forming the rim of the acetabulum and there is a tendency for the cancellous bone within the head of the femur to converge at an oblong focal area in the middle of the head. This fact emphasizes that the structure of cancellous bone is

(Conclusion of legend of Plate XII, on opposite page.)

understandable only when the bones forming the articulation are studied simultaneously as a unit and not when studied as isolated structures, separated from the normal relationship and function. The Gothic arch crucial structure of the ilium is produced by the ileus muscle mesiad and the glutei laterad.

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and repair stop when the dower of the proliferative energy of growth or reaction repair of the vascularized cells is equalized by the back-pressure of resistances to growth.

(b) What is the function of the blood supply?—The purpose of the blood supply is a balanced nourishment for the consolidated tissue, particularly the supply of inorganic salts in the normal proportions whereby the increasingly condensed tissue is able to maintain its integrity by reaction or adaptation to adequate pressure.

(c) What types of compression consolidate tissue?—The pressure of differential growth[2, 3] and the pressure of myogenic function. The pressure of differential growth is produced by the centrifugal expansion of confined and accelerated growing groups of vascularized cells restricted to a small volume by a limiting membrane which is relatively retarded in growth and that exerts a centripetal effect upon the central group of cells. The pressure is the resultant of skeletal cellular centrifugal growth meeting peripheral resistances that exert a centripetal action. This pressure of differential growth is manifested in the formation of myositis ossificans, dentine, and vegetative bone growth. This type of bone undergoes progressive atrophy when energy of growth, or repair following stimulus of trauma, is no longer manifested. This proliferation supplies the cells that are transformed into bone by pressure of differential growth. The myogenic function is the resultant of antagonistic reciprocal muscles in group action that produce the back-pressure vectors, transforming vascularized cells according to the parallelogram of forces. This type of bone, after growth ceases, maintains its integrity as long as there is adequacy of back-pressure by normal muscle function.

(d) What two fundamental factors, therefore, are involved in production and maintenance of bone?—(1) A biochemical factor; (2) a biophysical factor.

(e) What does the normal biochemical factor contribute to bone growth and maintenance?—It nourishes the confined growing and mature cells and supplies the chemical elements in balanced proportions out of which the bone substance is made by the cells reacting to an adequate pressure environment. The accelerated growing cells and peripheral resistances, together create this pressure environment.

The degree of hardness or density of the skeleton is directly proportional to its dynamic load or pressure and adequate nourishment. If the myogenic pressure be diminished by weak muscle tonus due to an unbalanced central, peripheral, or sympathetic nervous system, or inadequate blood supply, there will result decrease of skeletal consolidation by decompression and decrease in calcification and ossification. During maturity the skeleton is a pressure meter of muscle pull. The normal skeletal and muscular tissues are reciprocally dependent, both during growth and maturity.

The so-called vegetative bone growth is merely the manifestation of intrinsic rapid cell division, the resultant of the initial growth stimulus or the stimulus of trauma, against extrinsic resistances. This concept excludes from consideration the idea of a self-differentiated osteoblast; that is, a cell capable of secreting the osseous substance regardless of its environment. The bone secreting cell is *per se* a dependent cell that manifests bone properties in an environment

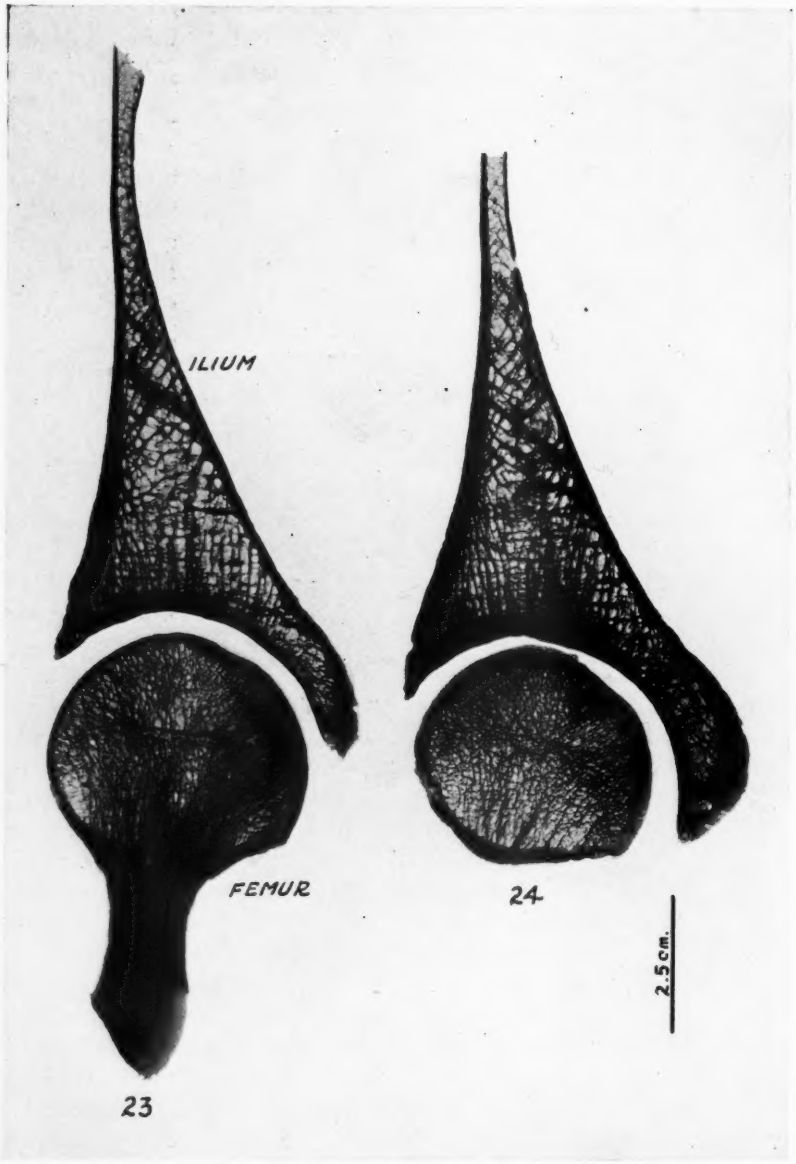

Plate XIII, Figs. 23 and 24. Roentgenograms of oblique coronal sections through the hip joint, ilium, head and part of neck of the femur. One-fifth reduced.

On the concave acetabular aspect of this joint the divergence of the cancellous bone is evident. These are plainly the continuation of those lines extending into the convex head of the femur at its middle oblong focal point. The transverse and oblique cancellous bone elements are more definitely related to the pressure stresses produced by abduction, adduction, medial and lateral rotation. Wherever the lines of pressure stresses cross many points of the same plane, such as the central oblong focal point of the head of the femur, the cancellous bone fuses into a denser plate of bone. The bone elements in the head of the femur end at right angles to the articular surface. Where the pressure stresses converge to form a smaller volume the cancellous structure converges to form compact bone, like the cortical bone of the neck of the femur. The converse also holds true, that compact bone passes into cancellous bone with an enlargement of the volume where the transmitted pressure stresses are constant.

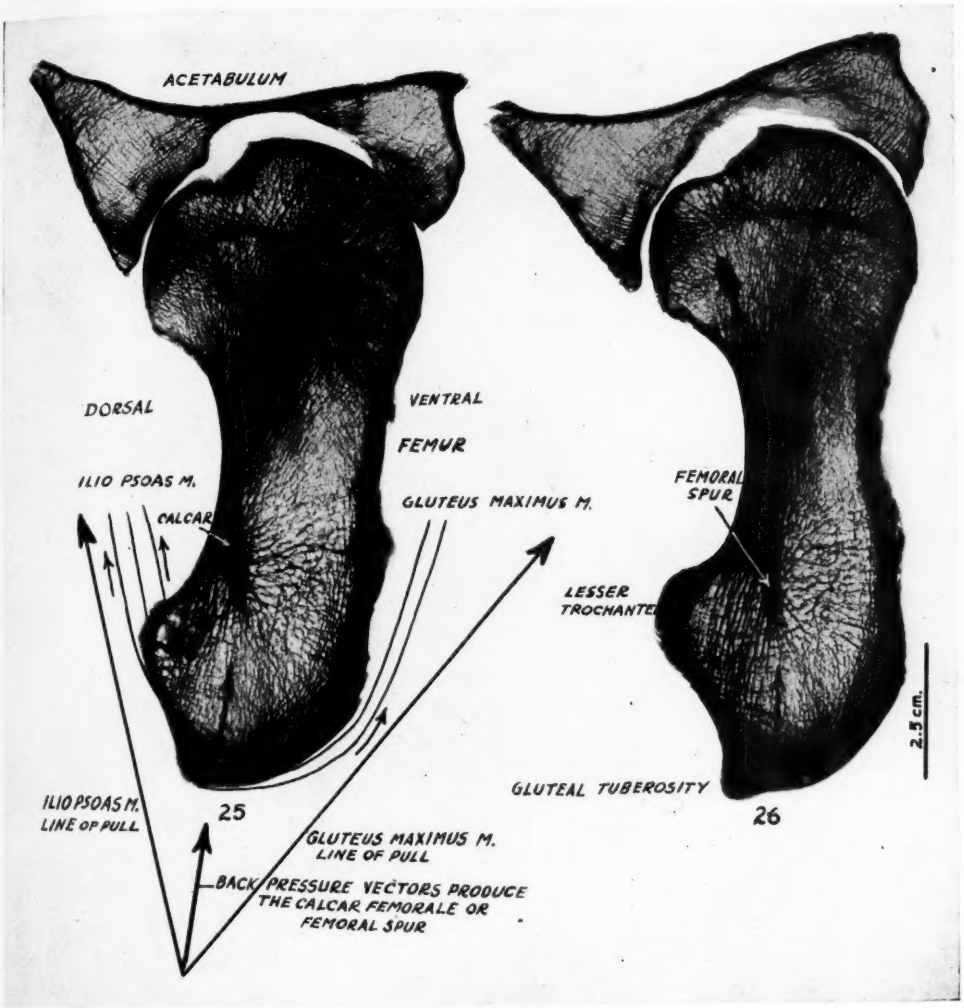

Plate XIV, Figs. 25 and 26. Roentgenogram of oblique transverse sections through the hip joint. One-fifth reduced.

The well-developed femoral spur of Merkel in the neck of the femur is clearly evident. This spur represents the condensation of bone that converges towards the dorsocephalic wall of the neck of the femur, produced by the back-pressure vectors of the ilio-psoas attached to the lesser trochanter and the gluteus maximus attached to the third trochanter. This femoral spur is one of the most striking examples of back-pressure vectors in the human skeleton. There is a striking example of a focal point of pressure in the head of the femur on the medial side of the fovea centralis represented by dense compact bone. The line of fusion between the epiphysis and diaphysis is represented by a dark line below the convex articular surface of the femoral head.

only of adequate pressure. First, the nourished reacting cell, and, second, the adequate environment together cause pressure and are the two essentials in bone production. The poorly nourished cell will lead to either no bone production or faulty calcium deposition.

Given, however, the most adequate nourishment and balanced proportions of inorganic salts in the blood stream, there will be

no reaction on the part of irritable cells to secrete hard bone substance unless there be an adequate stimulus for such a secretion. The calcium deposition is merely a protective adaptation or stiffening process, on the part of vascular mesenchymal cells, or vascular mesenchymal cartilage, against the increasing compression stimulus during the period of growth to mature maintenance: in the adult, equilibrium is established between the energy of growth and the back-pressure resistances to growth. This equilibrium is upset by injury.

(f) What does the biophysical factor determine?—It determines the adequacy of consolidation of tissue by pressure and the sites where the chemical elements will be secreted in the production of bone. The important point to stress is that consolidation of tissue is prior in time to bone deposition and that vascularization of consolidated tissue is likewise prior in time to bone formation. There are scleroblastemal and cartilaginous skeletons before the bony skeleton is formed. These three represent advancing degrees of consolidation reacting to a gradient increase of pressure.

(g) What bearing do these fundamental facts have on the problem of rickets?—These facts prove that there is a biophysical, as well as a biochemical, aspect to abnormal and normal bone growth. Alter the blood chemistry and normal proportions of the inorganic salts (Howland, Marriott, McKim, and Kramer[22] and the work of Shipley, Kramer, and Howland[23]) and inadequacy of chemical bricks results. A faulty construction is the sequela. Take away the adequacy of pressure of differential growth and myogenic function, and what results? There results inadequate tissue consolidation, therefore—the lack of an adequate stimulus for adaptation, which results in retarded transformation of cells into bone.

During the period of growth the reacting, vascularized mesenchymal cells enclose themselves in a hard case of calcium phosphate and carbonate. This is an adaptation reaction against an environment of pressure which is adequate to stimulate the cells to bone production. This environmental stimulus of compression is produced by differential growth and myogenic function. This compression stimulus determines the site of cellular consolidation and the continued adaptation of the condensed cells by calcium deposition. Hypomyotonia, by whatever cause, results in inadequate back-pressure or decompression of the skeletal condensed cells. This decompression of the adult skeletal cells results in halisteresis or chemical absorption of calcium salts. Decompression of the growing skeleton results in inadequate calcium deposition because of the insufficient compression stimulus. The degree of consolidation of the skeletal cells during growth and maturity under normal and abnormal conditions is a direct index or meter of the reaction of living protoplasm to an environmental pressure stimulus.

The dominant key that locks and unlocks the skeletal door to calcium deposition from the blood and absorption of calcium salts from bone into the blood stream is adequacy or inadequacy of the back-pressure vectors (compression and decompression) of normal and hypotonic muscle action and differential growth. The localization of back-pressure of adequate or inadequate back-pressure vectors and vascularized reacting cells are the fundamentals, the bed-rock, that determine the position or site of normal and abnormal bone growth, form and structural maintenance.

The presence or absence of cartilage in the callus formation subsequent to fractures

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22Howland, John W., Marriott, McKim, and Kramer, B.: Studies upon the Inorganic Composition of Bone. Jour. Biol. Chem., 1926, LXVIII, 721.

23Shipley, P. G., Kramer, B., and Howland, J.: Studies upon Calcification *in vitro*. Biochem. Jour., 1926, XX, 379.

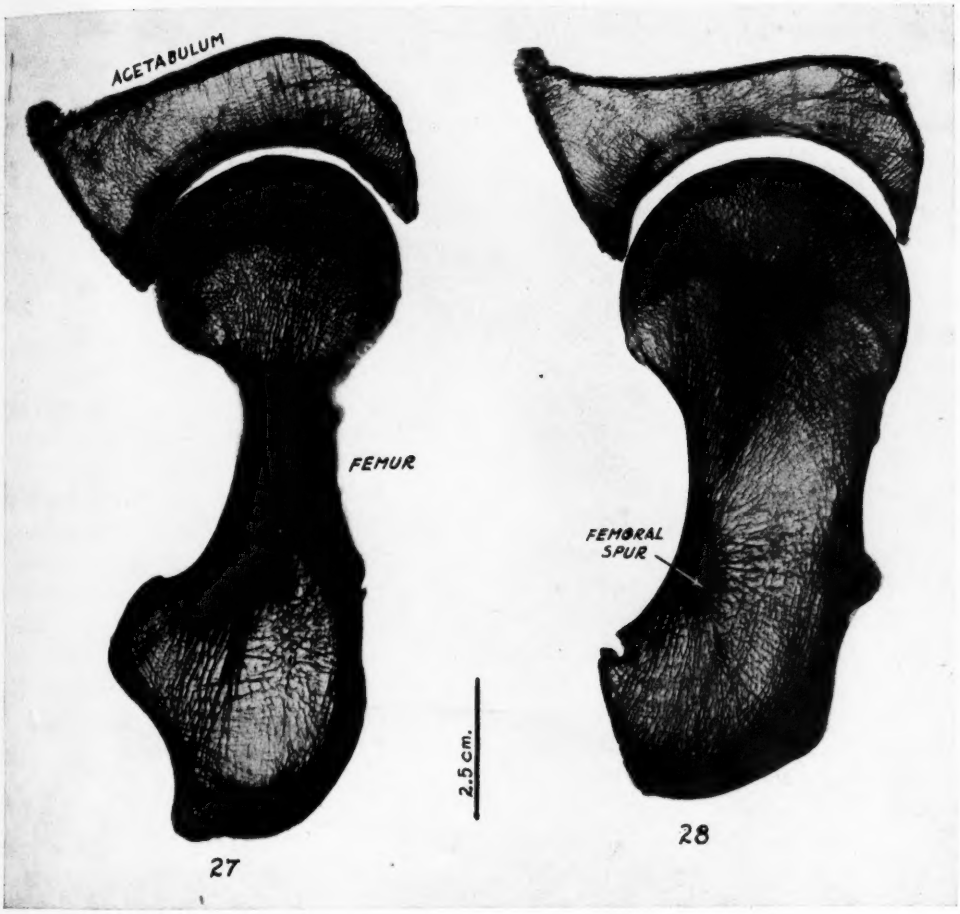

Plate XV, Figs. 27 and 28. Roentgenograms of oblique transverse sections through the hip joint. One-fifth reduced.

The calcar femorale or femoral spur of Merkel is a resultant of the back-pressure produced by the iliopsoas muscle attached to the lesser trochanter of the femur and the gluteus maximus attached to the third trochanter or the gluteal trochanter of the femur. See context for description.

(Bast, Sullivan, and Geist[24] and Harris[25]) is directly related to the volume of tissue repairing the gap and the degree of pressure brought to bear upon the vascularized cells bridging the breach of the bone. Given a constant pressure, the smaller the volume undergoing repair the sooner will adequate pressure for bone formation be induced; the greater the volume the more the cells will be subjected to a gradient pressure. Those cells occupying the larger volume will have a greater opportunity to experience that dimished degree of pressure adequate for initial cartilage formation as an intermediate stage. The large subperiosteal flange of the collar button callus has cartilage and occupies the greatest volume with relatively less pressure acting on a unit area of repair.

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[24]Bast, T. H., Sullivan, W. E., and Geist, F. D.: Anat. Record, 1925, XXXI, 255.

[25]Harris, H. A.: Bone Formation and the Osteoblast. Lancet, Sept. 8, 1928, p. 491.

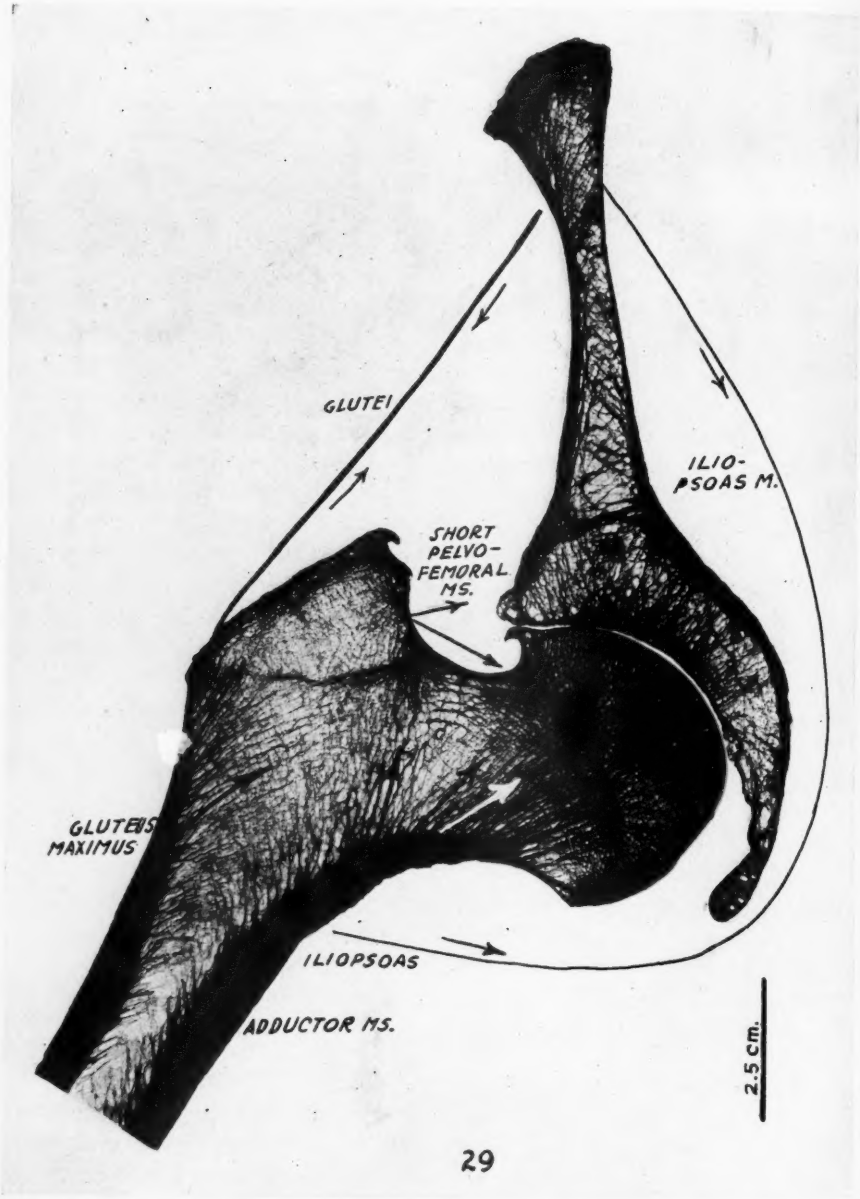

Plate XVI, Fig. 29. Roentgenogram of coronal sections through the hip joint, the femur, and acetabulum. The adductor, flexor group of cancellous trabeculæ on the concave medial aspect of the femoral neck are clearly evident. These are dominantly the resultants of the back-pressure produced by the adductor muscles and the ilio-psoas. Those cancellous trabeculæ on the convex aspect of the femoral neck, and related to the greater trochanter, are laid down by the dominant actions of abduction and extension of the hip joint. The short pelvo-femoral muscles, namely, the gamelli, obturators, and pyriformis attached on the medial aspect of the greater trochanter, produce back-pressure resultants along the convex aspect of the neck toward the acetabular articular head of the femur. The ilio-psoas and gluteus maximus muscles produce cancellous trabeculæ by the back-pressure of their actions toward the intertrochanteric or

(Conclusion of legend of Plate XVI, on opposite page.)

digital fossa on the medial aspect of the trochanter major. The intersecting back-pressure resultants visualized as cancellous bone in the ilium are produced by the ilio-psoas muscle mesiad and the glutei muscles laterad. The bones are in the position of abduction. One-fifth reduced.

Hill[26] states that strong muscles and firm bone are the result of exercise, fresh air, and diminished clothing, which aid in augmenting muscle tonus, in turn increasing skeletal pressure.

If, as postulated here, and elsewhere proved experimentally, normal bone is dependent on the normal unit function of the neuro-muscular-skeletal apparatus adequately nourished, then the alterations of the blood chemistry, the nervous system, and muscular tonicity are bound to affect the other integral part, bone, both during the period of growth and the period of maturity. The normal skeleton is a storehouse of calcium salts actively secreted by cells (Watt[27]) that are consolidated by compression of growth and muscle function. Hypomyotonia is one way of decompressing the skeletal cells and releasing the stored calcium through prolonged rest in bed, observed by every experienced roentgenologist. Emerson[28] observed a 20 per cent increase of serum calcium following ether anesthesia. Bauer, Aub, and Albright[29] noted a depletion of the calcium in cancellous bone trabeculæ by the prolonged administration of parathyroid extract. The bone trabeculæ, therefore, serve as a storehouse of readily available calcium. Brown[30] found that different intensities of light influenced the calcium and inorganic phosphorus content in the blood of rabbits. Hutchison[31] made clinical observations on osteomalacia in India, pointing to lack of muscular exercise as an etiological factor. He also came to the conclusion from clinical observations that early and late rickets were due to inadequate muscular development and function. Galbraith[32] confirms Hutchison's findings. Macht and Anderson[33] observed that ultra-violet irradiation by the ordinary or non-polarized waves with or without the addition of photosensitizing drugs, as sodium tetrabromfluorescein, in a series of patients with pernicious anemia has been followed by a definite improvement in the general condition. This observation, together with those mentioned above, shows the influence of an adequate environment upon the skin, nervous system, muscular tonicity, blood, and bone.

The clinical entity known as hyperparathyroidism, recently described by Barr, Bulger, and Dixon,[34] of St. Louis, has the following significant features:

1. Muscular weakness and hypotonia.
2. Abnormally high serum calcium.
3. Abnormal excretion of calcium in the urine and the formation of calcium stones.
4. Rarefaction of bone.
5. The occurrence of multiple cystic bone tumors, several of which on pathologic examination have been found to be giant-cell sarcomas.

The deposition of calcium salts, from the evidence presented, is apparently inextricably bound to the degree of skeletal consolidation by its action with immediate resistances that establish compression within

[26]Hill, L.: "On Clothes," Practitioner, London, December, 1928, CXXI, 359.

[27]Watt, J. C.: The Development of Bone. Archiv. Surg., December, 1928, XVII, 1017.

[28]Emerson, W. C.: Effect of Ether Anesthesia on Blood Calcium. Jour. Lab. and Clin. Med., December, 1928, XIV, 195.

[29]Bauer, W., Aub, J. C., Albright, F.: Bone Trabeculæ as Readily Available Reserve Supply of Calcium. Jour. Exp. Med., January, 1929, XLIX, 145.

[30]Brown, W. H.: Influence of Light Environment on the Calcium and Inorganic Phosphorus Content in the Blood. Jour. Exp. Med., January, 1929, XLIX, 103.

[31]Hutchison, H. S., and Stapleton, G.: Late Rickets and Osteomalacia. Brit. Jour. of Child. Dis., 1924, XXI, 105.

[32]Galbraith, J. D.: Muscle Tone in Rickets. Brit. Jour. Child. Dis., 1923, XX, 143.

[33]Macht, D. I., and Anderson, W. T.: Phototherapy in Pernicious Anemia. Jour. Phar. and Exp. Therapeutics, December, 1928, XXXIV, 365.

[34]Barr, D. P., Bulger, H. A., and Dixon, H. H.: Hyperparathyroidism. Jour. Am. Med. Assn., March 23, 1929, XCII, 951.

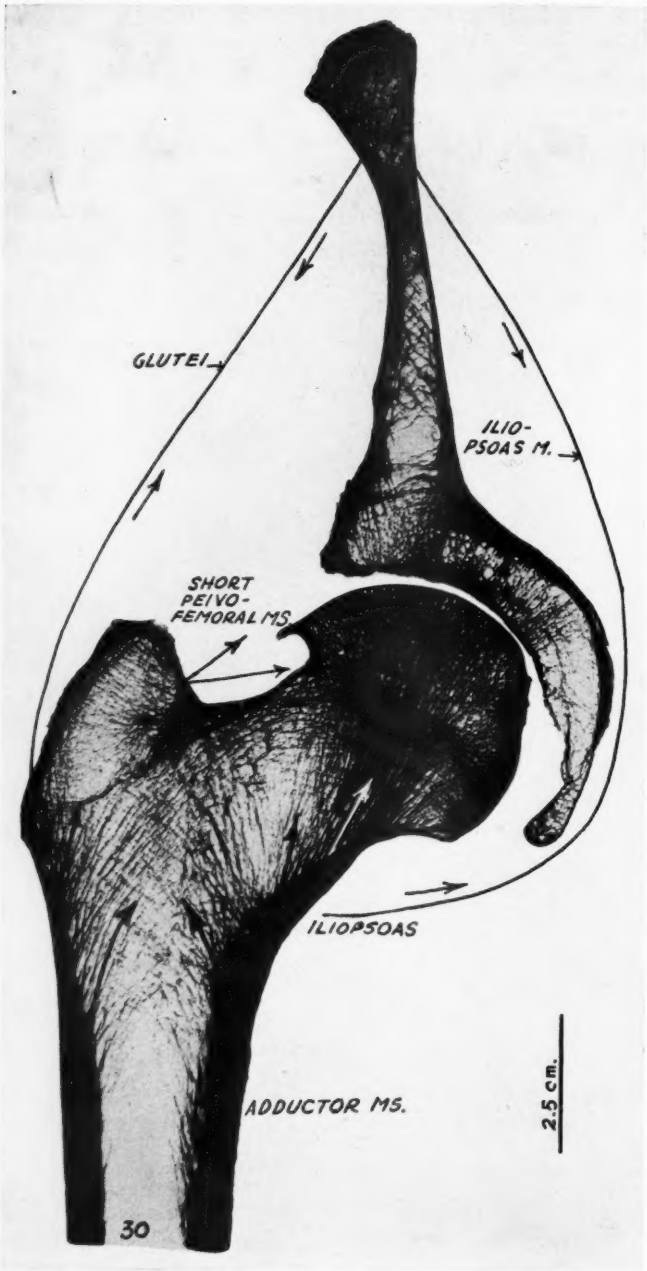

Plate XVII, Fig. 30. Roentgenogram of coronal sections through the hip joint, the femur, and acetabulum. The adductor, flexor group of cancellous trabeculæ on the concave medial aspect of the femoral neck are clearly evident. One-fifth reduced.

The bones are in the position of straight extension. There is balanced action between the glutei and ilio-psoas. The vertical trabeculæ on the concave side of the femoral neck are definitely related to the actions of flexion, adduction, and internal rotation, whereas the trabeculæ along the convex aspect of the femoral neck that pursue a more parabolic path than the above group are definitely related to abduction, extension, and lateral rotation of the hip joint. See context for explanation.

the skeletal zone. If the skeleton be decompressed by muscle weakness, hypotonia, or amyotonia, the serum calcium increases and is excreted in abnormally great amounts. There is concomitantly a depletion of skeletal calcium salts, visualized on the roentgenogram as skeletal rarefaction. The action of Collip's parathormone is evident first on the musculature, producing a hypomyotonia. This results in skeletal decompression and a flooding of the blood stream with calcium salts released by the decompressed bone-producing cells, with the lifting of the adequate compression that initially stimulated the undifferentiated cell to be a bone-producing one.

The mobilization of calcium salts is evidently determined by the degree of muscle tonus. With a normally developing muscle tonus during growth and maintenance of this tonus during maturity, the deposition of calcium salts in the skeleton is maintained at a normal rate and amount. When the normal back-pressure in the skeleton produced by normal muscle tonus is abnormally reduced by hypotonus or muscle weakness, the pressure-reacting skeletal cells give up their calcium salts, with the reduction or elimination of the skeletal pressure stimulus. The metabolism of calcium salts as regards the degree of skeletal density is evidently directly proportional to the degree of back-pressure produced by muscle action in maturity, with the addition of the pressure of differential growth during the growing period.

In parathyroid tetany (hypoparathyroidism) the biological phenomena are related to hypertonus, with depletion of the blood stream of calcium salts by increased skeletal consolidation. The muscular tetanic condition causes prolonged increase of back-pressure on the skeleton and skeletal response by greater adsorption of calcium salts and resultant increased consolidation, which depletes the blood stream of its available calcium salts. In hypoparathyroidism calcium is adsorbed from the blood stream at a faster rate than the normal one of ingestion of calcium salts because of increased skeletal consolidation by back-pressure of tetanic musculature. In hyperparathyroidism, the reverse occurs; that is, calcium is given up to the blood stream by the decompressed bone cells at a faster rate than it is excreted. Consequently, there is an abnormally high content of blood serum calcium due to the calcium flood into the blood stream by the decompressed skeleton, caused by marked muscular relaxation, weakness, hypotonia, or amyotonia produced by many factors.

The writer has had experiments on dogs under way for the last twelve months on localized ablation of muscles from various parts of the skeleton. These will be reported at a future date, but I may state that evidence at hand points to skeletal decompression by muscular excision as one immediate cause for giant-cell sarcomas. The multiple cystic bone tumors and giant-cell sarcomas associated with conditions of hyperparathyroidism are the resultant of decompressed skeletal cells and the concomitant disorganized growth, the result of hypomyotonia or amyotonia, as proved in the experiments on dogs.

During growth, early and late rickets may be produced by hypomyotonia, which, in turn, has multiple etiological factors. The resultant decompression of the skeleton by a failure of the normal muscle action to produce its back-pressure vectors leads to retardation of the consolidating process, with continued cellular proliferation. In other words, the normal rate of bone differentiation does not keep pace with skeletal cellular proliferation because the adequate compression stimulus is diminished or lacking. There result, then, relatively soft enlargements, occupying larger volumes — the rosary and swollen epiphyses.

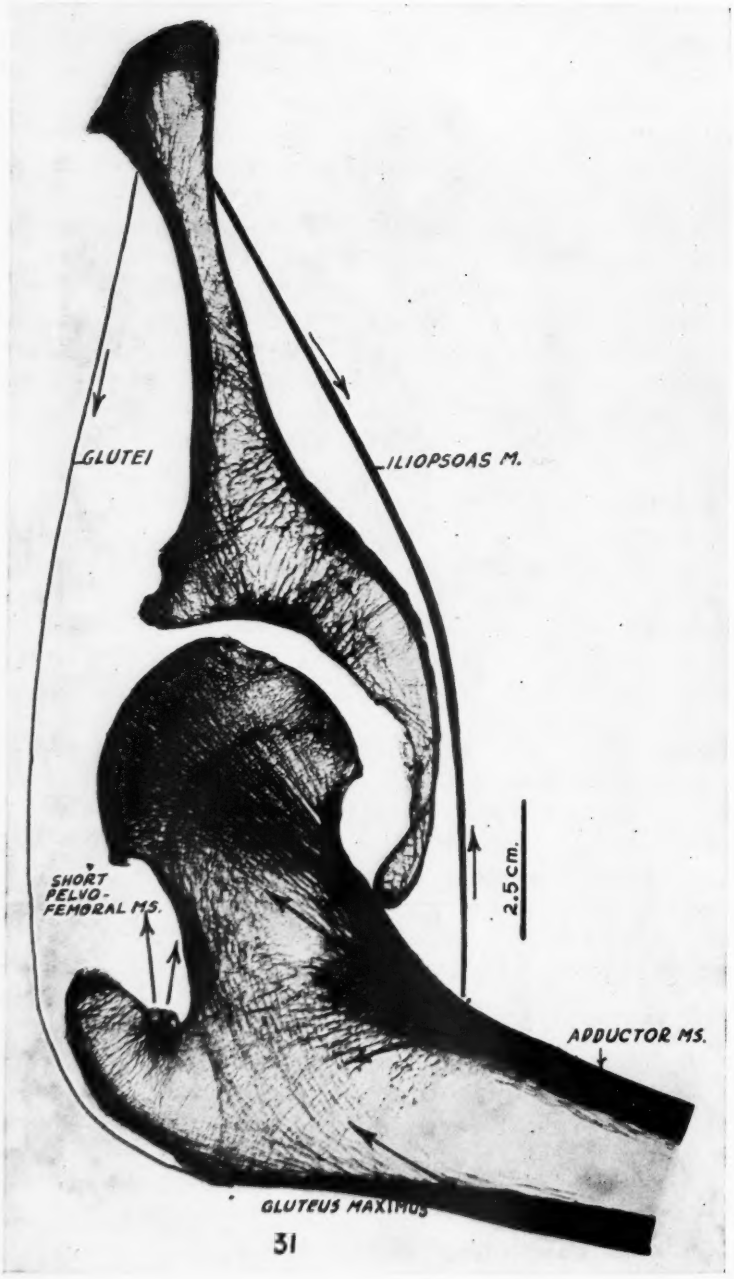

Plate XVIII, Fig. 31. Roentgenogram of coronal sections through the hip joint, the femur, and acetabulum. One-fifth reduced. The bones are in the position of hyperadduction. The vertical trabeculæ on the concave side of the femoral neck are definitely related to the actions of flexion, adduction, and internal rotation, whereas, the trabeculæ along the convex aspect of the femoral neck that pursue a more parabolic path than the above group are definitely related to abduction, extension, and lateral rotation of the hip joint. See context for explanation.

During the mature period, after growth ceases, the maintainer of the normal skeleton is the related muscles in action. The maintainer of the normal skeletal muscles is the related joint-segmented rigid bases of origin and insertion between which there is a capacity for motion—the skeleton. One may not exist under normal conditions without the other. Normal skeletal bone and muscles are reciprocally dependent tissues, therefore, and not merely the products of close structural relationship of two distinct independent tissues. The clinician viewing the musculature and skeleton from the dynamic, in contrast to the static, viewpoint, in the light of action or function, sees a locomotor apparatus that constitutes the unit for motion, made up of mutually dependent, interacting part , of alternating, reciprocal, muscular engines (Sir Arthur Keith[35]) that apply their forces on a rigid base, segmented by joints. No part of this unit locomotor apparatus may be affected without affecting the whole.

I am convinced that this functional conception of the unit neuro-muscular-skeletal locomotor apparatus adequately nourished, instead of the purely structural one of unit skeleton and unit musculature, brings into harmony the varied theories, apparently diametrically opposed, that have been advanced to explain the etiology of rickets. These theories are as follows:

1. The fat-soluble vitamin theory of Mellanby[36] and McCollum.[37]

2. The calcium-phosphorus imbalance theory of Howland, Marriott, Kramer, and Shipley.[22, 23]

3. Deficient ultra-violet light of the sun.

4. Lack of fresh air and the environmental hygienic theory of inadequate muscular exercise leading to hypotonia, of Hutchison,[31] Galbraith[32] and others of the Scotch school, first described by the English anatomist, Glisson,[38] in 1650 (Jackson, 1925[39]).

The fundamental physico-chemical condition for absorption of calcium salts, in areas of calcification in dead hyaline tissue (Wells[40]) and the active secretion (Watt[27]) of calcium salts in peripheral intercellular places, is tissue consolidation, the result of compression leading to an absolute or relative decrease in volume relative to the force of the compressing agent. Harris[41] states: "It seems that until the chemist explains the colloidal processes which lead to the deposition of the salts of calcium in two tissues so fundamentally distinct as dying cartilage on the one hand and living bone on the other, we must continue to regard the osteoblast as a splendid being, endowed with genius, sensibility, and intelligence, ever ready to perform the work at hand."

This conception of the osteoblast expressed by Harris endows the so-called osteoblast with powers of forming bone regardless of environment; in other words, the osteoblast is considered as an intelligent self-differentiated cell. Harris' paper is an excellent one, but the conclusion quoted above is at variance with that presented by the writer in this paper. The bone cell is considered by the writer to be a product of position or environmental pressure in the organized embryo. The internal environment of tissue organization, of differential growth and developing muscle function produce in confined vascularized cells consolidation by compression. The bone cell is, according to this concept, a de-

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35Keith, Sir Arthur: Menders of the Maimed. Oxford Press, London, 1919, p. 106.

36Mellanby, E.: Rickets. Lancet, 1919, CXCVI, 407.

37McCollum, E. V.: The Vitamin Hypothesis. Jour. Am. Med. Assn., 1918, LXXVII, 937.

38Glisson, F. (1650): Abstract, St. Bartholomew's Hospital Rep., London, 1884, XX, 71.

39Jackson, C. M.: Inanition and Malnutrition. Blakiston, Philadelphia, 1925, p. 133. This monograph summarizes the subject in an excellent manner.

40Wells, H. G.: Pathological Calcification. Jour. Med. Research, 1906, IX, 491; Calcification and Ossification. Harvey Lectures, 1910-11: Calcification and Ossification. Archiv. Int. Med., June, 1911, VII, 721: Chemical Pathology, 3d ed. W. B. Saunders Company, Philadelphia, 1918.

41Harris, H. A.: Bone Formation and the Osteoblast. Lancet, Sept. 8, 1928, p. 499.

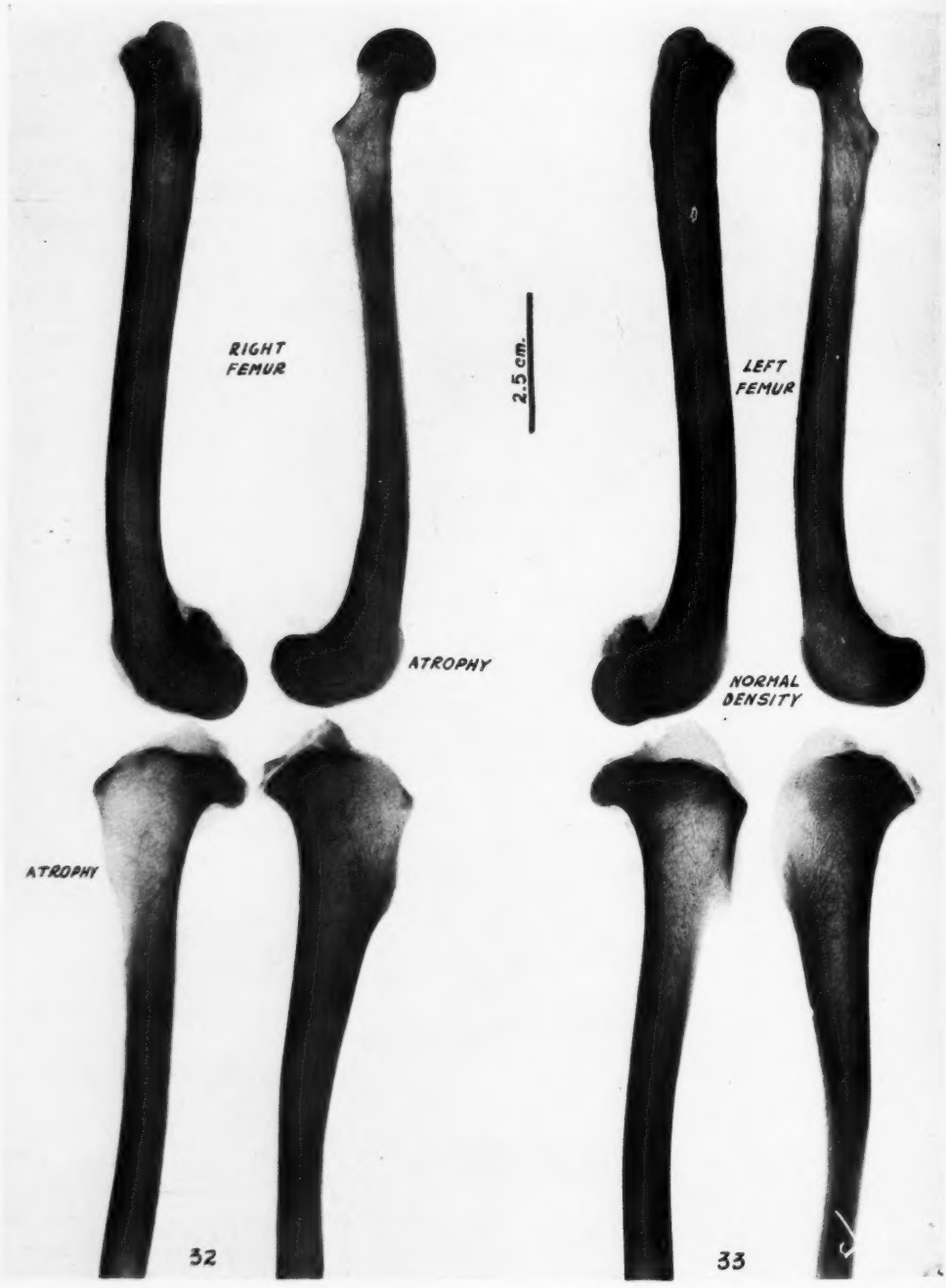

Plate XIX, Figs. 32 and 33. Roentgenograms of sagittal sections of the femur and tibia of an adult dog. One-fifth reduced.

The right quadriceps extensor femoris muscle was surgically excised under aseptic conditions 2.5 cm. proximal to the patellar attachments. There was no marked disturbance of the periosteal or epiphyseal

(Conclusion of legend of Plate XIX, on opposite page.)

blood supply. The portion between the incision and the insertion of the muscle into the tibia, including the patella, was excised. The operation occurred seven weeks prior to the time that the roentgenograms were made. There were twenty-four dogs used in this experimental series and only the earliest of these observations is here presented. After the operation the stifle joint of the right leg was hyperflexed and the dog used the left hind limb for locomotion. Seven weeks is a short period of time in which to observe marked bone atrophy. It is definitely evident that on the ventral aspect of the right tibia and the patellar aspect of the right femur the cancellous trabeculæ belonging to the extensor system produced by the quadriceps extensor femoris muscle have undergone considerable atrophy in comparison to the corresponding locations of the left tibia and femur by the local exclusion of a muscle. There is a focal atrophy of bone, therefore, corresponding to the local missing back-pressure vectors of action of the excised muscle. This fact is most strikingly observed after longer periods of time have elapsed from the date of muscle excision.

pendent one, not intelligent or an independent free-lance to form bone, but dependent on chemical factors and physical factors—the result of body organization.

The "intelligence" manifested in originating muscle and bone and molding them to function belongs, not to bone or muscle as independently growing tissues, but to the plan or organization, the dynamic blueprint of the primordial germ cell. This active organizatory factor (Eldridge[42]) leading to structural expression is called by Aristotle "entelecy," and is defined by Hans Driesch[43] as "order of relation." Skeletal bone is a product of compressive relationship produced by the mutual antagonism of confined and condensed vascularized cells growing against peripheral resistances, the result of differential growth and the functional back-pressure of the tonic and more active muscle tug. This biophysical concept of the osteoblast eliminates a rôle of independent bone origin in any cell in the body. This concept aids in understanding metaplasia of young growing vascularized cells into paraskeletal bone as an interaction of the growing cells of repair and its immediate extrinsic environment. The origin and maintenance of bone are dependent on chemical and physical factors dominated by body organization. This organization may be upset by injury from any cause.

Dean Lewis[44] studied cases of bone formation in laparotomy wounds, and because the participation of the periosteum was excluded, inclined to the view that these parosteal bone masses were due to metaplasia. This view of the etiology of abnormal, as well as normal, bone I believe to be the true one. After injury, if the biophysical conditions be adequate, as well as the chemical ones, organizing young growing connective tissue cells of repair and initial growth will be transformed into bone.

What are these biophysical conditions?—(1) The rapid proliferation of (2) confined condensed vascularized cells growing against a (3) developing circumscribed and limiting membrane (Macewen[45]) produced by differential growth. (4) The centrifugal expansion of the central confined and vascularized cells and the (5) centripetal effect of the peripheral resistances, together produce the adequate compression of differential growth for vegetative bone origin. This bone maintains its integrity as long as the reactional energy of the original growth or repair reaction to stimulus of injury is manifested by cellular proliferation. When proliferation ceases, due to the establishment of equilibrium with the resistances produced by the surrounding soft parts the bone of myositis ossificans traumatica usually undergoes progressive osteoporosis due to the lack of bone-maintaining functional pressure. The production of a hematoma stimulates the accelerated growth of cells

42Eldridge, S.: The Organization of Life. Crowell Company, New York, 1925, p. 244.

43Driesch, H.: The Science and Philosophy of the Organism. 1910, II, 169.

44Lewis, Dean: Myositis Ossificans. Jour. Am. Med. Assn., May 5, 1923, LXXX, 1281.

45Macewen, William: The Growth of Bone. Glasgow, J. Maclehose and Sons, p. 28, 1912.

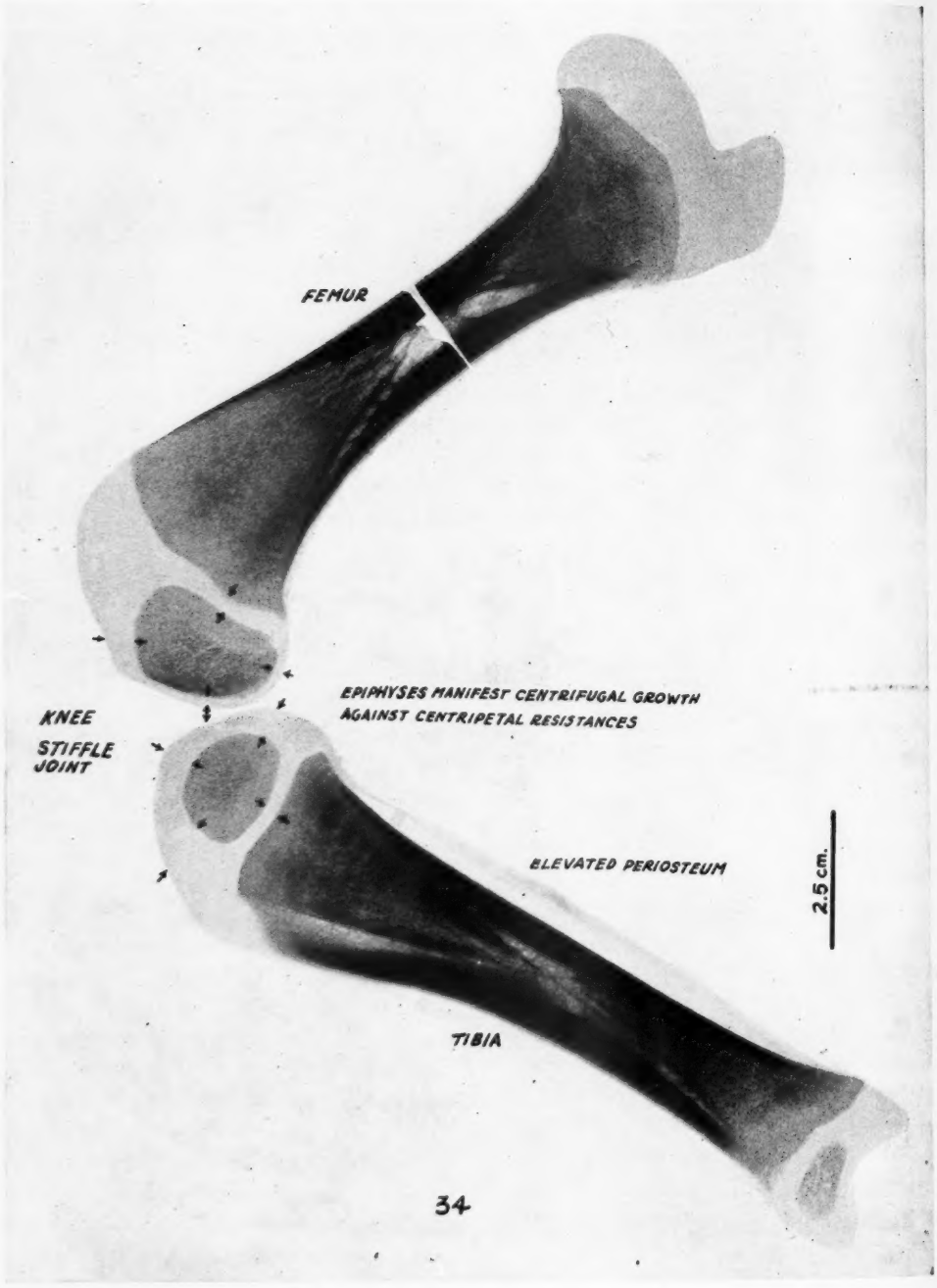

Plate XX, Fig. 34. Roentgenogram of sagittal sections of the femur and tibia of the fetal cow. One-fifth reduced.

In the ungulates there is marked epiphyseal and muscular development of the skeleton prior to birth. At the time of birth in the case of the cow the epiphyses are as far advanced in development as in

(Conclusion of legend of Plate XX, on opposite page.)

the human of twelve to fifteen years of age. The plane of section through the head of the femur which is in the coronal plane was just lateral to the epiphyseal bone. This section of the femur corresponds to the development illustrated in Plate XXI, Fig. 37. The epiphyseal bone represents a terminal pressure system segmented from the diaphysis. It forms the hub of converging back-pressure systems in joint mobilization. In addition to this functional back-pressure there is the pressure of differential growth manifested by the centrifugal expansion of proliferating cells against peripheral centripetal resistances.

when the nutrition is adequate, resulting in differential growth.

On the other hand, adequate vascularization of the accelerated growing cells and the subsequent tensional membrane formation restricting this growth are consequently physical conditions necessary for the origin of bone of differential growth. There is, then, a transformation of multipotent vascularized dividing mesenchymal cells into skeletal or paraskeletal bone. It is this environmental biophysical relationship, producing compression, that underlies the metaplastic changes of young connective tissue cells into bone. There is no need to postulate, therefore, migrating or extruded osteoblasts for the production of bone in normal or abnormal sites.

This viewpoint does not deny that in bone formation, in certain abnormal zones, the osteogenetic layer of the periosteum may be involved, but, if it be so, there is the adequate production of the compression environment due to differential growth or no bone forms. There is no cell in the body, if this concept of bone origin and formation be true, that has the intrinsic endowment connoted by the generally accepted definition of the term "osteoblast"—of independent bone formation, regardless of environment. It is the environment, fortunately, over which the clinician has limited control.

What guides or controls structural expression from the dynamic blueprint stage to maturity? What controls order of relation? These questions remain unanswered by the chemist and physicist. The architect or engineer of bone origin and structure is not, according to the writer's interpretation of the morphological and surgical experimental facts, herein presented, a property of the osteoblast, but an attribute of the relativity, of interaction of primitive skeletal cells and the surrounding soft parts. The bone cell is a product of this interaction that produces compression consolidation of confined vascularized cells, the resultant of differential growth and myogenic function. The active secretion of calcium salts by the cells called "osteoblasts" is an environmental adaptation to the back-pressure vectors which are stimuli of confined cells of differential growth and muscle function.

FUNCTIONAL INTERDEPENDENCE AND MORPHOGENESIS

The interpretations derived from the objective evidence presented in this paper are in harmony with the modern functional and etiological tendency of morphological studies to-day. The purely descriptive, static phase of morphology was necessary during the infancy of the science, but the morphologist is now making an earnest attempt to explain by experimental means the factors underlying the genesis and maintenance of the external form and internal structure of the parts of the body. This is well expressed by Streeter[46] for the vascular system; Stockard[47] for morphology in general, and Swann[48] in emphasizing the relation of physics and vital processes. Evans[49] has identified a growth- and a maturity-pro-

[46]Streeter, George L.: Archetypes and Symbolism. Science, April 29, 1927, LXV, 405.

[47]Stockard, Charles R.: The Trend of Morphology. Science, April 5, 1929, LXIX, 363.

[48]Swann, W. F. G.: Physics and Vital Processes. Science, Nov. 2, 1928, LXVIII, 411.

[49]Evans, Herbert M.: Antagonism of Growth and Sex Hormones of the Anterior Hypophysis. Jour. Am. Med. Assn., Nov. 3, 1928, XCI, 1337.

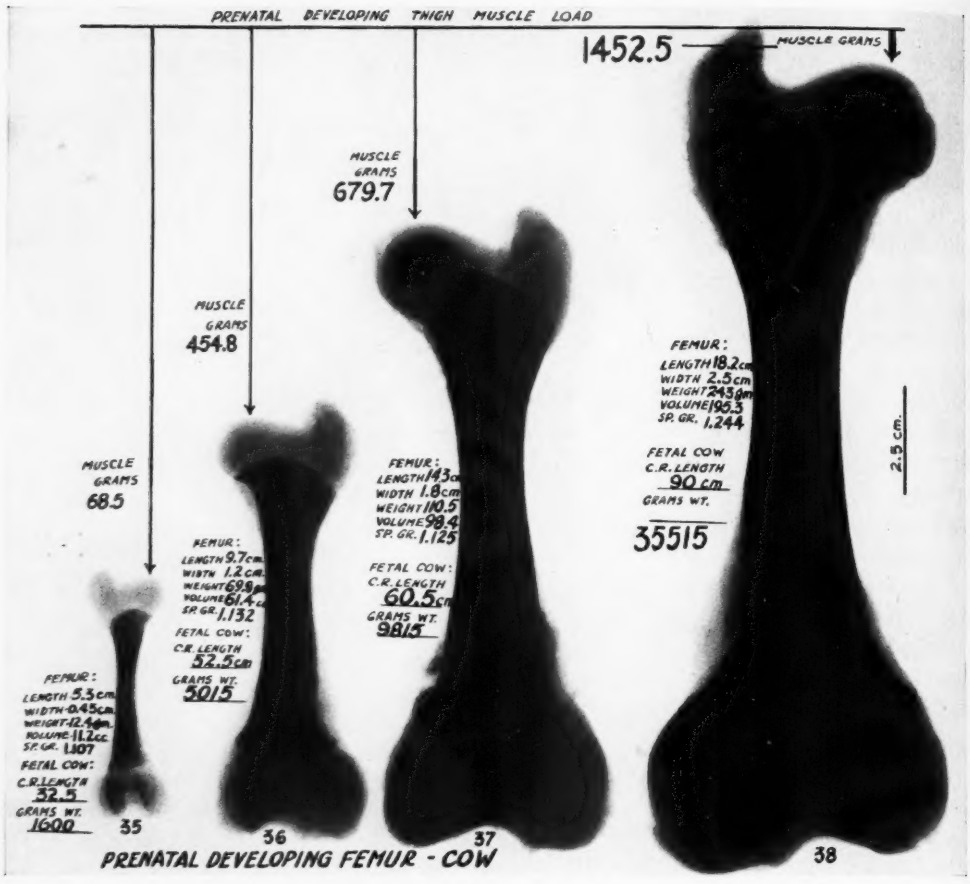

Plate XXI, Figs. 35 to 38. Roentgenograms of the developing stages of the femur in the fetal cow. Two-fifths reduced.

The femur in Fig. 38 is from that of a fetus about one week prior to birth. The evaluation of the facts enumerated in this plate are the following: (1) In the 90 cm. fetal cow the femoral length is approximately three times greater than that in the 32.5 cm. cow; the weight, however, increases 20 times. (2) Relatively, the femoral length in the 90 cm. fetal cow to thigh muscle weight is approximately 6 times shorter than that of the 32.5 cm. fetal cow. (3) The femur in the 90 cm. fetal cow would be approximately 42 inches in length instead of 7 inches, if the ratio of femoral length to thigh muscle weight in the 32.5 cm. fetal cow were maintained up to the 90 cm. stage of development. (4) The weight of the femur increases in about the same proportion as the weight of the musculature, and there is an absolute increase in density corresponding to the thigh muscle development. (5) The musculature, therefore, apparently hammers down and relatively shortens the femur during the growing period; at the same time femoral weight and density are increased corresponding to muscle development. The development of the musculature, and peripheral nervous system and epiphyseal bone in the cow at birth correspond to that in the human at twelve to fifteen years of age. (6) The volume of the femur during prenatal development decreases relative to its weight.

voking hormone from the hypophysis, as well as a vitamin associated with sex processes, and Scammon[50] the growth interrelationships of the various organs of the body by statistical methods. Jackson[39] has presented an excellent study on malnutrition and inanition in relation to morphological changes, as well as mathematical evidence of the interrelationship of organs during growth. The pioneer classical study of

[50]Scammon, R. E., and Ness, Marie M.: Changes in the Amount of Certain Constituents of the Human Body in Prenatal Life. Anat. Rec., March 25, 1929, XLII, 35.

Gudernatsch[51] on the relationship of the thyroid to changes of body form are well known. This work has been extended by many investigators. The association of the hypophysis to changes of body form is being placed on firm scientific ground by Smith[52] and Evans[53] and by Zondek and Aschheim.[54]

Excellent work has been done on tissue culture of primitive cells with the aim of revealing the autonomy or the extent of the potencies of cells for self-differentiation, initiated by Harrison[55] and extended by Warren and Margaret Lewis,[56] Carrell and Burrows.[57] The pioneer observation of Harrison definitely points to a limited dependent differentiation of the neurone in the growth of the nerve fiber. Harrison emphasizes the relationship of a flat contact surface (a solid support or cellular stereotropism), in order that this growth extension of a nerve fiber may occur, which means that in the organism the interaction of parts is important in the expression of neurone form. This same condition is emphasized by the Lewises in their tissue culture work of cross-striated muscle and intestinal sympathetic nerve fibers.

Harrison[55] states (on page 190 *l. c.*): "Change of form and locomotion may be readily observed in tissue culture, but only when the cells are in contact with solid support (cellular stereotropism)." In the same article (on page 191) Harrison continues: "The specimens were mounted in the following ways:

"1. In clotted hen plasma.

"2. In defibrinated plasma but supported by spider web.

"3. In a hanging drop of defibrinated plasma so small that the tissue remained in contact with the cover slip.

"4. In a large hanging drop without contact with the cover slip or any other solid support.

"In a preparation of each of the first three classes characteristic movement of cells of a number of different kinds of tissue took place, while in the fourth the tissue remained inert."

In the cultivation of sympathetic nerve fibers W. H. and M. R. Lewis conclude as follows: "The fibers creep along on the under side of the cover slip; they probably are stereotropic." The solid support *in vitro* of the cover slips takes the place of developing neighboring parts within the embryonic body *in vivo*. The work of the Lewises on "Behavior of Cross-striated Muscle in Tissue Cultures" (1917, page 173 *l. c.*) shows the relationship of muscle growth to stereotropism as follows: "The muscle outgrowths occur either in the form of muscle buds that are continuous with the cut ends of the muscle fibers or as free fibers which wander out into the medium among the mesenchyme cells on the under surface of the cover slip."

Riddle[58] has stressed the functional interrelations of the hormones and especially the relation of basal metabolism to the experimental control of sex. Males are characterized by high and females by low basal metabolic rates. These facts are important because there is a close functional interrelationship between the different times of sexual

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51Gudernatsch, J. F.: Am. Jour. Anat., 1913-14, XV, 431; Anat. Rec., 1916-17, XI, 357.

52Smith, P. E., and Graeser, J. B.: Anat. Rec., 1924, XXVII, 219; Smith, P. E.: Anat. Rec., 1926, XXXII, 221; Foster, G. L., and Smith, P. E.: Hypophysectomy and Replacement Therapy, Jour. Am. Med. Assn., Dec. 25, 1926, LXXXVII, 2151; Smith, P. E.: The Disabilities Caused by Hypophysectomy and their Repair, Jour. Am. Med. Assn., Jan. 15, 1927, LXXXVIII, 158.

53Evans and Long: Anat. Rec., 1921, XXI, 62; Proc. Nat. Acad. Sci., 1922, VIII, 38; Evans, H. M.: Harvey Lectures, 1923-24; Evans, H. M., and Simpson, Miriam E.: Anat. Rec., 1925, XXIX, 356; 1926, XXXII, 206; March 25, 1927, XXXV, 36.

54Zondek and Aschheim, S.: Deutsche med. Wchnschr., Feb. 19, 1926; Ztschr. f. Geburts. u. Gynak., 1926, XC, 372.

55Harrison, R. G.: The Cultivation of Tissues in Extraneous Media as a Method of Morphogenetic Study. Anat. Rec., April, 1912, VI, 181.

56Lewis, Warren, and Lewis, Margaret: The Cultivation of Sympathetic Nerves from the Intestines of Chick Embryos in Saline Solution. Anat. Rec., January, 1912, VI, 7; Behavior of Cross-striated Muscle in Tissue Cultures. Am. Jour. Anat., Sept. 15, 1917, XXII, 169.

57Carrell, A., and Burrows, M. T.: Present Condition of a Strain of Connective Tissue Twenty-eight Months Old. Jour. Exp. Med., 1914, XX, 50.

58Riddle, O.: Some Interrelations of Sexuality, Reproduction and Internal Secretion. Jour. Am. Med. Assn., March 23, 1929, XCII, 943.

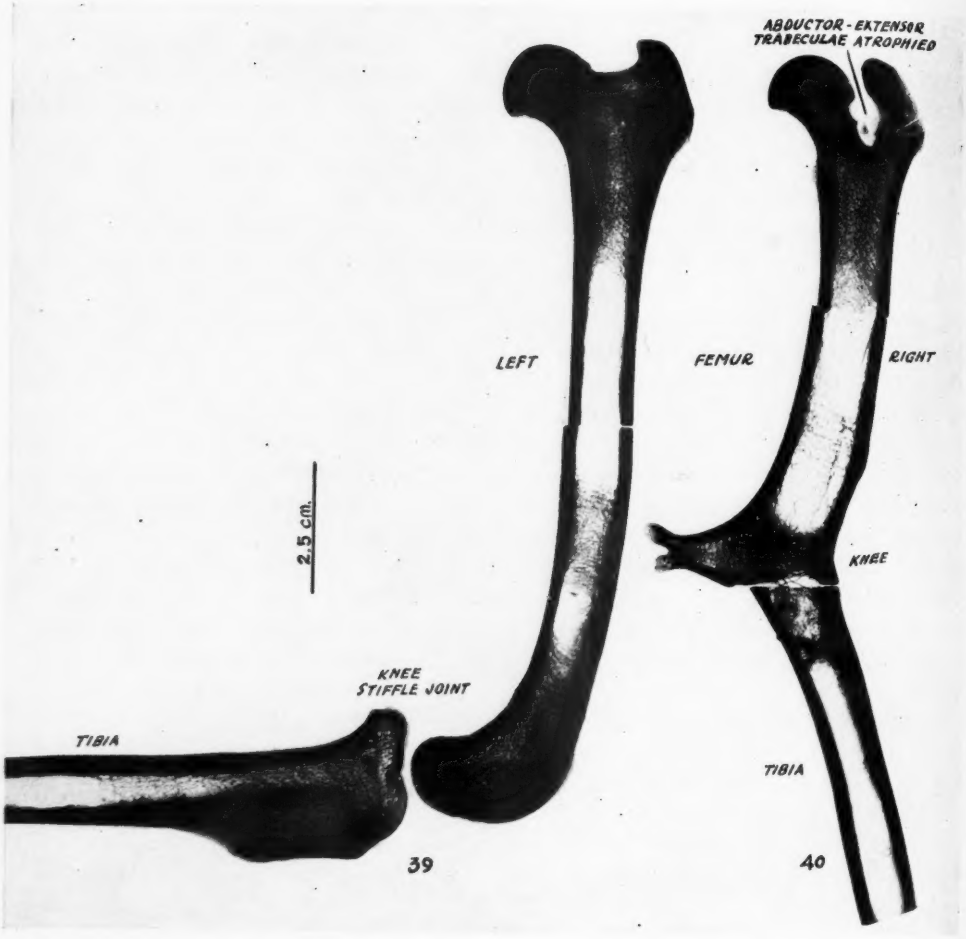

Plate XXII, Figs. 39 and 40. Roentgenograms of the left and right femora and tibiæ of a mature dog. One-fifth reduced. Mid-sagittal sections, 2 mm. thick, of distal one-half of femora and tibiæ; coronal sections of proximal one-half of femora.

The right knee joint was fixed under aseptic surgical conditions by wire, February 29, 1928, when the dog was five months old. There were eight puppies in this series. All the dogs lived and the results are identical. In Plate XXII the roentgenograms are of the bones of dog No. 123, killed February 16, 1929. The dog No. 123 lived 351 days subsequent to operation. The knee joint was opened from the lateral aspect; a slight amount of articular cartilage of the femur and tibia was removed and the wire inserted through a drill hole, 1 cm. proximal to the distal femoral epiphyseal growth plate and 1 cm. distal to the proximal tibial plate. The blood supply was not fundamentally disturbed at time of operation. With subsequent growth and progressive premature fusion of the epiphyseal femoral and tibial bones with one another and with their respective diaphyses there is alteration in the pattern of the blood vessels. By immobilization at the dog's right stifle or knee joint there is an alteration of the extensor and flexor pattern of the cancellous trabeculæ in the femur and tibia at the knee joint. The limb, after removal of the plaster-of-Paris cast ten days subsequent to the operation, was held in the position as regards the hip joint of hyperflexion and hyperadduction under the dog's abdomen. The relation of the femur with the tibia was that of hyperextension. The dog used the left hind leg for locomotion. Because of inhibition of the extensor and abductor action at the hip joint, the muscles producing these actions were markedly atrophied compared with those on the left side. The abductor-flexor trabeculæ on the convex aspect of the bent right femoral neck were markedly atrophied compared with those of the left femoral neck. These experiments and the results presented in Figs. 39 and 40 are definite proof of the cause-effect relationship of hip and knee cancellous bone architecture with the back-pressure vectors of muscle action in normal joint range of mobilization.

The factors that determine the appearance of a segmented epiphyseal bone are the following: (1) in-

(Conclusion of legend of Plate XXII, on opposite page.)

tensity of pressure of differential growth of vascularized mesenchymal cartilage; (2) intensity of back-pressure vectors of muscle action which depend on (3) the degree of muscular development in relation to the degree of skeletal development and (4) joint range of mobilization. This does not mean that the mobile joints of all vertebrates necessarily must possess bony epiphyses, for the intensity of the terminal epiphyseal pressure produced by adequate muscle action is likewise a determining factor, as well as the joint range of motion that consolidates the hub-like epiphyseal compression zone at the end of the long growing bone. H. B. Fell (Osteogenesis in the Domestic Fowl. Jour. Morph. and Physiol., 1925, LX, 417) states there are modified epiphyses in the developing bones of the chicken, except at the tibiotarsal joint, which is typical. Transverse sections were studied through the mid-femoral and right ankylosed knee joint regions.

maturity and that of the musculature and skeleton in the male and female.

The interaction of the primitive parts of the limb in developing to maturity and the necessity of considering the limb as a functional unit made of parts that are mutually dependent for locomotion may be seen by the results obtained in the transplantation experiments of Detweiler[59] and his students and by Swett.[60]

In a series of studies begun in 1915 by the writer[2] it was first proved that the musculature was capable of spontaneous and stimulated movements in a specific direction as soon as it was differentiated in the living pig embryo. It was also proved that the musculature was active during the rotation of the hind limbs and that the activity of the progressively developing muscles influenced osteogenesis. This work on the early activity of the developing muscles has recently been confirmed in the living rabbit embryo in Eliot R. Clark's Laboratory by Swenson.[61] The earliest formation of primary bone in the mammalian body is influenced by the related musculature that first differentiates and manifests action.

Even the living fertilized zygote of the rabbit dividing *in vitro,* shown before the anatomists at the University of Rochester, New York, March, 1929, by Warren Lewis in a beautiful moving picture of the changes to about the thirty-two-cell stage, is under the restraining organizing influence of the primitive peripheral *zona pellucida.* At the time of cell division there is a tendency for the cells to fly apart. They exert marked tension on the *zona pellucida* at the telophase of mitosis, but are prevented from open separation by the restraining, confining, *zona pellucida*-limiting membrane. When this spherical membrane was punctured by accident, the central confined cells were extruded and underwent rapid disorganized growth. While observing these dynamic changes I immediately compared the limiting influence of the *zona pellucida* on the growth of the rabbits' blastomeres with that limiting membrane, the blastemal one or perichondrium (periosteum) in restraining and aiding in organizing the growth of the contained proliferative cells that undergo progressive structural changes as growth advances, objectively evident, as (1) the scleroblastemal, (2) cartilaginous, (3) osseous skeletal stages.

The radiologists who observed the excellent Canti film, shown in Chicago, Dec. 5, 1928, will remember the rapidity of growth of the subperiosteal cells of the seven-day chick embryos in tissue culture, when relieved of the surrounding periosteum. At the termination of telophase the two daughter cells separated and immediately, on division of the mother cell, were projected widely apart to opposite poles by some repelling influence. These cells in tissue culture had lost the inhibitory physical restraint

[59] Detweiler, S. R., and Carpenter, R. L.: An Analysis of the Mechanism of Co-ordinated Movements in Heterotopic Limbs. Anat. Rec., March 25, 1929, XLII, 14.

[60] Swett, F. H.: Regulation in Cartilaginous Shoulder-girdle Grafts. Anat. Rec., March, 1929, XLII, 40.

[61] Swenson, E. A.: The Active Simple Movements of the Albino-rat Fetus: The Order of Their Appearance, Their Qualities and Their Significance. Anat. Rec., March 25, 1929. XLII, 40.

of a limiting environment. The daughter cells of Rous' chicken sarcoma also lost the capacity of contiguous relationship. The dynamic ebullition of the cytoplasm just prior to cell division and the explosive separation of the two daughter cells at the telophase, normally, must be restrained, confined and limited if organization is to be orderly and progressive. The Canti film of disorganized subperiosteal growth and growth of Rous' chicken sarcoma, and the Warren film of organized and disorganized growth of the rabbits' blastomeres have convinced me of the correctness of the view of the limiting influence of the periosteum on the central accelerated growing group of cells first emphasized by Macewen[45] for postnatal life and by Carey[2] for pre-natal life as a tension fibrosis.

Evidence in these films has also firmly convinced me of the "dynamics of histogenesis" in relation to muscle, joint, and bone, which I have had to reconstruct and visualize in motion from static stages of advancing development in microscopic observation of fixed material. The moving picture in five minutes has visualized processes for others, who, because of lack of familiarity with the specific static microscopic evidence, could never see motion in fixed material, no matter how closely graded the advancing stages of development may be.

Organized as well as disorganized growth is closely bound up with the biophysical factor of mechanical restraint, namely, membrane formation. This was formerly expressed by Ribbert[62] in his tissue-tension theory of neoplasms. Many etiological factors may destroy the restraining structures that limit rapidly growing cells to their normal organized sphere of action, such as mechanical, thermal, chemical, bacterial agents. Under normal conditions the individual organization stubbornly resists any injurious agent that tends to upset its equilibrium and quickly seals the breach or welds the gap by an ultimate adequate fibrosis-membrane formation. These conceptions are in harmony with the prevalent one of Bloodgood,[63] Wells,[64] Maude Slye[65] and others, that disorganized growth is first local, due to chronic irritation, and that a weakened constitution through inheritance is unable to cope adequately with the wear and tear of the immediate environment of the chronic stimulation expressed by the term "chronic irritation." When the normal dynamic factors of histogenesis are clearly understood we will have less confusion in understanding disorganized growth of cells.

Many clinicians have presented evidence in variable amounts that sustains the thesis that the bone-producing cells of growth or repair following trauma derive their attributes as a cellular reactional adaptation or response to an environmental stimulus that consolidates the cells by compression, namely, Allison and Brooks,[66] Bancroft,[67] Bloodgood,[63] Bucholz,[68] Coley,[69] Ely,[70] Haas,[71] Hess,[72] Henderson,[73] Kolodny,[74] Lewis,[44] Phemister,[75] Ryerson,[76] and many others.

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CONCLUSIONS

1. The architecture of mature cancellous bone at monaxial, biaxial, and triaxial joints is determined by the back-pressure vectors of muscle action in joint range of mobilization and not by the static load of body weight.

2. During development there is a pressure of differential growth that results in so-called "vegetative bone formation" in addition to that of muscle action. The origin of bone is a stiffening process of confined and richly vascularized mesenchymal cells enclosed by a circumscribed membrane, and involves the accelerated proliferation of cells growing centrifugally in a relatively small volume against a limiting extrinsic, centripetal resistance. The interaction of the centrifugal and centripetal factors of differential growth creates intra-embryonic environmental pressure. This is known as the allelocatalytic effect or the mutual acceleration of the growth of cells dividing in a relatively small volume by the catalyst of growth. The failure to produce bone by tissue culture *in vitro* is due to the facts that the pressure of structural organization has been eliminated, and that the so-called "osteoblast" has been regarded as a self-differentiated cell capable of forming bone regardless of its environment. Bone produced by differential growth, such as myositis ossificans, usually undergoes atrophy, when energy of repair is equalized, if no functional pressure be brought to bear upon the bone.

3. Selective focal atrophy of cancellous bone groups in the adult dog may be accomplished experimentally by the local surgical excision of the muscle whose back-pressure vectors resulted in the structural expression of specific groups of cancellous trabeculæ.

4. During the prenatal development of the femur in the fetal cow there is a relative shortening of the femur sixfold in relation to thigh muscle weight from the 32.5 cm. to the 90 cm. stage, as well as decrease in femoral volume relative to femoral weight. The femoral weight and density increase in direct proportion to the thigh muscle weight. The femur is apparently hammered relatively shorter and more consolidated during the prenatal period by growth resistances, especially the back-pressure of the developing tonic thigh musculature. The mature skeleton is a pressure-meter of muscle pull.

5. The calcar femorale or femoral spur, in the neck of the human femur, is the objective expression of the confluent back-pressure vectors which are the resultants of the actions, primarily, of the extensor gluteus maximus and flexor ileo-psoas muscles of the hip in sustaining body weight in the erest posture.

6. The normal growth and mature structure of cancellous bone is the result of a dynamic muscular activity and the intrinsic capacity of skeletal cells to proliferate centrifugally against extrinsic centripetal resistances. The normal skeleton and related musculature are reciprocally dependent and mutually interactive in origin, growth, and mature structural maintenance. The adequately nourished and functional skin, nerves, muscles, tendons, bones, and joints form a functional unit for motion.

7. The value of rest as a therapeutic agent following fractures is variable for each bone in the body and is dependent on the extent of injury. Rest is primarily of value during the reparative period of proliferation following injury. The stimulus of trauma supplies the cellular bricks that weld the gap of the fracture. The subsequent value of motion, after the vascularized cells have adequately filled the breach, is the adequate conduction of back-pressure vectors that accelerate the transformation of the vascularized cells into bone and pre-

vent excessive callus formation. The time for motion and its execution should be under the strict guidance of the clinician.

8. The osteoblast is a dependent cell that acquires its morphological attributes by the position it occupies in the developing embryo or zone of repair in the adult: it is a reaction cell adequately nourished, and consolidated by the stimulus of compression of structural organization, during the period of differential growth and functional mature maintenance. The site of active secretion of calcium salts by the cells called "osteoblasts" is the location of an environmental adaptation by young growing or repairing vascularized cells to the back-pressure vector stimuli of differential growth and muscle function.

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THE USE OF RADIUM IN THE TREATMENT OF NEVI[1]

By ZOE ALLISON JOHNSTON, M.D., PITTSBURGH, PA.

IN the consideration of this subject there are some interesting points to be brought out. I will mention briefly the types of nevi to be considered, other methods of treating nevi, and the experience of other workers, spending more time on the technic of treatment and end-results obtained after radium treatment.

Nevi, as the name indicates, are usually present at birth. It has been estimated that 33 per cent of new born infants are so afflicted. Some nevi are fully formed at birth and do not seem to increase in size, except as they increase with the growth of the body; others are so small at birth as to be inconspicuous, but some time later show marked development. They may consist of areas of hyperplasia of the superficial capillaries or of the arteries or veins, or there may be an excessive deposit of pigment. Nevi are generally considered to be developmental defects, appearing sporadically without any hereditary tendency.

Four common types of nevi are considered and they are named according to the type of tissue which predominates. (1) *Nevus flammeus*, or port wine mark, consisting of dilated capillaries; (2) *nevus vasculosus*, usually consisting of dilated arteries; (3) *angioma cavernosum*, consisting of inter-communicating blood spaces of abnormal size, usually of venous origin, and (4) *nevus pigmentosus*, consisting of abnormal tissue with an excessive amount of pigment. The last classification includes those with or without pilosis.

These lesions are sometimes most disfiguring. The color may vary from a pale pink to a deep scarlet. They may be purple or blue, or, in the pigmented type, a very ugly brown. Some of the angiomata cavernosa show such an over-development of tissue as to be repulsive. Treatment is undertaken in order to remove or to shrink up as much of the abnormal tissue as possible, with a minimum of damage to surrounding areas, and to leave as healthy and inconspicuous a scar as possible.

Wickham and Degrais are considered the pioneers in this work; at least, up until the time they published their book in 1907, nothing of any value had been published on this subject. Electrolysis had been almost the only method in use. This was painful, required repetition, and could not be used upon nevi of any considerable size. These authors reported a large number of birthmarks treated successfully. Since that time many methods have come into use, but radium still is the method of choice in a large percentage of such cases.

In the consideration of other methods of treatment desiccation and electrocoagulation have a limited field. They are sometimes used in cases of nevus vasculosus, if the lesions are not too large, in preference to any other method. They are also used in the removal of the pigmented moles. McLean and Cannon mention the successful use of desiccation in the treatment of port wine marks. If one wishes to eradicate tissue which will not shrink up under radiation therapy, desiccation is probably the first choice.

Carbon dioxide snow has been very popular, but, from the literature, I do not believe that many are using it at the present time. Its application is painful, is followed by a severe reaction, and there is a possibility of the formation of thick unsightly scars. Eller reports splendid results with carbon dioxide in port wine marks. McLean

[1]Read before the Radiological Society of North America at the Thirteenth Annual Meeting, at New Orleans, Nov. 28–Dec. 2, 1927.

and Cannon treat the circumscribed raised vascular nevi very successfully with carbon dioxide snow.

Surgery has been found highly unsatisfactory in the treatment of most types of birthmarks. It has been tried out thoroughly in some of the vascular and angiomatous types, but, on account of the danger of recurrence and scarring, is probably not of great value. Surgery may have a place in the removal of small pigmented nevi, but better cosmetic results are obtained by other methods.

The roentgen rays do not seem to act as favorably as the rays from radium. A small dose of X-ray does not seem to be as beneficial to a birthmark as a similar small dose of radium.

The Kromayer lamp, which is a modification of the Cooper-Hewitt generator, has been used in the treatment of port wine marks. Some writers report excellent results. The treatment must be given frequently over a long period of time. In order to accomplish anything, a rather severe reaction must frequently be produced. This treatment is trying both to the physician and his patient.

A very interesting article was published in *Acta Radiologica,* March, 1927, by Gunnar Andren, summarizing the work at the Radiumhemmet, 1909-24. He puts special stress on the healing effect of radium in these cases, not through necrosis, but through regression which may occur without reaction. The most of the work was done with radium: some cases were treated with X-ray, but poor cosmetic results were reported. Electrocoagulation was substituted for radium in the treatment of the pigmented type. In the port wine mark, or "hæmangioma capillare," as he calls it, good results were obtained only when the patient was treated while under one year of age.

Pusey states that either X-ray or radium is the better method of treating flat vascular nevi, but the results are only partially successful.

The experience of Morrow and Taussig in treating vascular nevi shows that their results with radium are better than with carbon dioxide snow or any other therapeutic agent. Radium therapy is most satisfactory for nevus vasculosus; next, for cavernous angioma; least, for nevus flammeus.

The beta rays should be utilized as much as possible: with proper technic, severe reactions should not occur.

According to Stevens, elevated, tuberous, or cavernous nevi respond well to radium. He has been using radium plaques for this purpose since 1910, cross-firing where possible. He concludes that radium in small quantities over long periods of time gives satisfactory results in raised or cavernous hemangiomata.

Kirby-Smith obtained his best results in the removal of port wine birthmarks with carbon dioxide snow and radium. In nevus pigmentosus he believes that either radium or X-ray gives the best cosmetic and the most lasting results.

Eller believes that radium is the treatment *par excellence* for angioma cavernosum and that it gives by far the best cosmetic results. In most cases, with the proper technic, no scar will remain. The dose should be just a little less than the amount required for a first degree reaction and it may be repeated every four to six weeks. This author believes that radium is by far the treatment of choice for nevus vasculosus. He believes that X-rays and radium are absolutely contra-indicated in the treatment of port wine marks. In their removal by irradiation, either with or without filtration, unsightly scarring is unavoidable, with more or less atrophy, keratosis, and pigmentation.

Montgomery and Culver consider screening of the greatest importance, believing

that it is far better to err on the side of screening too much rather than too little. This is especially important from the standpoint of the cosmetic result. They report a number of cases of nevi treated with radium in which excellent results were obtained.

Molesworth speaks very favorably of the roentgen-ray and radium treatment of nevi. He believes that it is desirable to begin treatment while the nevus is small and still growing, in which case an almost perfect result may be obtained with X-rays or radium. The end-results in the cases treated by carbon dioxide snow are not so good as those produced in even the more obstinate cases treated by means of radiation.

The effect of radiation on blood vessels is described by Pinch (1920) in the following way: Prolonged intensive radiation produces proliferation, with subsequent vacuolarization and degeneration of the endothelium, infiltration by leukocytes of the vessel wall, and finally stenosis of the vessel lumen. Weak and brief radiation at long intervals causes proliferation of the endothelial cells, fibrosis of the vessel wall, and finally stenosis of the vessel.

TECHNIC

We do not have any fixed technic in the treatment of nevi. It must be adapted to the need of each individual case. The type of lesion must be considered, because superficial radiation may be used in one case and more heavily filtered radiation in another. The size and location of the lesion must be taken into consideration. If a birthmark happens to be situated in the scalp a certain type of radiation should be used. The age of the patient must be taken into consideration. The duration and frequency of the application of the radium depends so much upon the lesion. This will be brought out in the discussion of each type.

In the nevus flammeus, or capillary type, radium does not seem very successful. Any radiation treatment produces a mottled result and sometimes the patients are worse off than before treatment was started. If one could have a radium applicator the exact size of the lesion, giving an even distribution of the radium, such a condition could possibly be avoided. This, however, is impossible in the majority of these cases. Tubes or plaques used over the surface of the lesion are bound to overlap or leave a space between areas, which produces this mottled result. A rather severe reaction must be given to these types of lesions or there will not result any tissue change. These heavy reactions are so often followed by atrophy, discoloration, or dilated vessels.

The cases coming under this type which we have observed were treated by the section method. A section or part of the birthmark was given an application of radium. We use vanadium steel needles each containing five or ten mg. of radium; 1 mm. of rubber is used for filtration. The radium was distributed as evenly as possible over the section to be treated. The application was left in position long enough to produce a moderate reaction. The second section or part was not treated until the reaction had disappeared in the first section. The remaining sections were treated in the same manner. Treatments were not repeated under two or three months. In most cases the electric needle or desiccation was used to remove objectionable vessels or discolorations.

Nevus vasculosus is the type which we might say is ideal for radium treatment. An opening is cut in a piece of lead foil the exact size of the lesion. A radium applicator is made from tubes or needles, placing them from 1.5 to 2 cm. apart, according to the strength used. We try to give a dose which will produce a slight, not a severe, reaction.

These nevi fairly melt under radium treat-

ment, and, if too large a dose is not used, very satisfactory results may be obtained. These treatments, like the others, it is best not to repeat under two to four months. We have a round plaque with a surface of 1 sq. cm. containing 5 mg. radium which is convenient to use in the small elevated vascular nevi which we often see. If the nevi are thick enough, or if they are situated near the eyelids, radium needles can be inserted. Wherever it is possible, we like to insert radium needles. One treatment consisting of buried radium takes the place of a number of superficial applications, and we are less likely to have atrophy and scarring.

The angiomata cavernosa, if very large and extensive, are treated by rather heavily filtered radium, or by the insertion of radium needles. We use 50 mg. of radium, filtered with 1 mm. of brass and 1 mm. of rubber. If large areas are to be treated, a sufficient number of these tubes are used to cover the area. If the angioma is very thick, we use felt to increase the distance of the radium container from the surface of the lesion. Radium needles are really ideal, because a more even radiation can be obtained throughout the lesion. We never have had any bleeding that could not be stopped by pressure, or did not stop within a few minutes of its own accord.

Pigmented nevi are difficult to treat. Radium therapy does not play such an important part in the treatment of these as it does in the case of vascular nevi. Epilation, leveling of projections, and decolorization are the main effects. In some cases the decolorization is incomplete. We use an application of radium over the entire surface of the nevus, giving dosage sufficient to produce a rather severe reaction. This is repeated in two months, if it seems necessary. The tissue shrinks considerably, and, after the reaction has entirely disappeared, the area is desiccated. Scarring can hardly be prevented in this type, but with cautious handling it is possible to have only an inconspicuous scar.

Treatment should be started as early in the infant's life as possible. When superficial applications are to be made, we like to begin at six to eight weeks of age. The dose used is small and we have never noted any general reaction. When needles are to be inserted, we wait until the babies are at least six months old. This may not be necessary, but we have always felt that there is more likelihood of reaction when needles are inserted.

Since so many nevi are situated about the face, we are especially interested in cosmetic results. From experience we know that excellent cosmetic results can be obtained in the vascular type and in the cavernous angiomata. Fair cosmetic results are obtained in many of the pigmented nevi, while we get a rather unsatisfactory result in the port wine marks. Our aim is not only to cause the disappearance of the birthmark, but to produce the least possible scarring.

SUMMARY

1. Radium therapy, properly applied, is beneficial in a large number of cases. It becomes a menace only when our enthusiasm leads us to over-dosage.

2. Experience has taught us to select the treatment for each individual case. Best results are often obtained by a combination of methods.

3. Radium in the treatment of the great majority of birthmarks shows a degree of usefulness, varying according to individual cases, that is incontestable.

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DISCUSSION

Dr. G. W. Grier (Pittsburgh, Pa.): I am glad of an opportunity to again express my admiration for Dr. Johnston's beautiful work on birthmarks. While I have never had the temerity to treat birthmarks with the insertion of needles, her results show that in the hands of those familiar with such technic the results are very beautiful. There is possibly a safer method for one who does not do a great deal of that kind of work: it is surface application with well filtered radiation. It is my belief that the final results will be just as good if one uses brass filtration and there will be less danger of surface reaction. In young babies—and these cases are usually presented for treatment when the baby is quite young—one must be very careful that he does not produce surface reaction, for it is easy for a baby's skin to become infected. In one instance in which there was a very large birthmark on the baby's cheek, I saw the whole cheek slough open as a result of the baby scratching the cheek with his finger nails after it had had a good sized dose of radium treatment, but a dose that would not have caused any damage but for this superimposed infection. One must always remember that the larger the birthmark the greater the effect will be with a milligram-hour dosage of radium. If one is treating the whole cheek by covering it with twenty-five milligram packages, one will not dare to leave that radium on as many minutes as he would if he were using only one or two capsules of radium. This must be remembered, for instance—counting that one knows that his dose is two hours with a certain technic, with a single package of radium, if the whole side of the face is covered and that radium left on for two hours, he will certainly get into trouble.

Another point I feel should be stressed is that the time between treatments should be generous, and, personally, I never treat inside of eight weeks—never repeat the treatment inside of eight weeks. It takes a long time for these changes to occur inside of the blood vessels and for fibrosis to take place. Your final cure will not be hastened by treating the case at shorter intervals, and the danger of after-consequences will be much less if you allow good wide intervals between the treatments.

Dr. James M. Martin (Dallas, Texas): To begin with, I know very little about the subject. I do occasionally treat a case of birthmark with radium. I have had some very good results and some results of which I am not particularly proud. In all probability, my failures were due to faulty technic, because I have not had enough experience in that particular line of work to feel always sure that I am doing exactly the right thing. I have learned, however, that the dose, as in everything else, is of first importance and must be as nearly right as possible, because following the treatment of some of my early cases there developed a telangiectasis that was almost as ugly as the birthmark itself. This condition was due, I think, to a lack of proper filtration; and this thought has helped to develop the belief that X-rays should be filtered too. I never use an X-ray dose of any intensity without filtration. However, that is off the subject just now.

Most of the cases of birthmark that I have cured with radium have been in babies. I have refused to treat adults because a few

cases have not resulted satisfactorily. Dr. Johnston knows a good deal more about this particular line of work than I do, and I take off my hat to her for what she is doing; but I am sure she will occasionally get unfavorable after-effects—I believe we all do. I have seen several cases that had been treated by others, where the after-effects were not altogether what they should have been. The cases were all improved, and, of course, if one can improve an ugly condition on the face, it is worth while. However, I think it is a pretty good idea to have a definite understanding with the parents of the child before the treatment is begun, because when they come to consult you, they are expecting you to take the blemish off their child, and unless you have a definite understanding with them, they are going to be very badly disappointed if you fail in any degree. I have nearly a thousand feet of motion pictures that I have made of cases before and after treatment. Some of them show splendid results and some I am not proud of, and I have not been showing these pictures because they are not very complimentary.

I cannot pass this opportunity to say a word about filtration of X-rays. I think I tried to make that clear yesterday. Dr. Grier[1] and I do not agree on that point, but again I want to take off my hat—this time to Dr. Grier—because he is doing good work. I am using half a millimeter of aluminum filtration in the X-ray treatments for superficial skin lesions, and my reason is simply this: years ago, when I began doing X-ray work, I used no filtration whatever, and I am constantly meeting cases, showing ugly telangiectasis, that I treated in those days. I do not feel happy when I meet them and I would like, in passing, to make an observation. I treated a woman about ten years ago, over the shoulder and on the neck for malignancy after operation, and she is going around happy and well with a large mark that looks worse than a birthmark. About five years ago her mother developed a similar condition in the shoulder, for which a doctor in a nearby town referred her to me. I filtered my rays and gave her a good many more treatments than her daughter received, and the mother has no evidence of telangiectasis. This is just one case in many that I might mention. I am very much ashamed of the daughter's condition because I think I could have prevented it. I believe that unfiltered radiation favors telangiectasis, and that is the reason I am using filtration in all cases.

I cannot miss this opportunity, also, to defend the multiple dose method. I have tried the single dose method over and over again, and nearly always failed. I want Dr. Grier to teach me how to cure epithelioma in one dose. The multiple dose method has given me far better results, and I want to say that the method I use is a massive dose method, an accumulated massive dose method, and a method that should be thoroughly understood or not used, because it leads one close to the borderline. In the treatment of cancer we are perfectly justified in pushing our method to the limit, because we are dealing with a condition which, if not cured, will soon become fatal.

Dr. Rollin H. Stevens (Detroit, Mich.): Dr. Johnston's paper on the use of radium in the treatment of nevi has been exceedingly interesting to me, because I have been doing more or less of that work for the last twenty-five years. My first experience was in using the Finsen light on port wine birthmarks on the face. I was young and enthusiastic in those days, had just returned from Copenhagen with a Finsen light apparatus, and was willing to put in a good many more hours of treatment then than later. After twenty-five years some of that

[1] Dr. Grier's paper, Surface Applications of Radium, was published in Radiology, December, 1928, XI, 474.

enthusiasm has disappeared, and I am not willing to spend quite so much time, but I must say that the results in those cases treated with the Finsen light properly applied were highly satisfactory, though almost all the cases I treated then were women of twenty to thirty years of age. The color of the nevi was very much lessened in intensity, and in one or two cases it almost completely disappeared. Later on, when I began to use radium, I treated small areas of port wine stains in babies, and secured very good results. We did not have to produce a reaction. I tried to keep away from a reaction and simply gave a very small dose with a small amount of radium to small nevi —not more than 2 cm. in diameter. Many of those disappeared without showing any reaction or any scar, but they were very slow in going away. One dose was usually all I gave—sometimes a second dose would be given after three or four months—but it would take a year or longer for the nevus to disappear—there was no scar left. When, however, one applies radium to the larger port wine nevi—more than one or two centimeters in diameter—the results are negative; I have never had any satisfactory results in treating those cases with radium. All nevi respond better to radium treatment in very young children than in adults.

Now, the vascular nevi we treat with radium quite successfully, trying to avoid severe reaction. I have never used the needles in nevi—have no experience whatever with that—but we have had very good results with surface application, using radium plaques, or plaques made up from radium needles, well filtered and quite a distance from the skin. In pigmented nevi I always use radium because of the possibility of malignancy developing. The radium does not diminish the pigmentation, but rather increases it. The pigment can be destroyed by means of desiccation or carbonic snow.

DR. I. GERBER (Providence, R. I.): I would like to ask Dr. Johnston to tell us a little more about the technic she uses with the needles. Inserting needles into nevi is necessarily different from the procedure used in cancer. My own experience, and I suppose that of most of us, in inserting radium needles has been limited largely to malignancies. I would appreciate it if Dr. Johnston would mention something about the upper and lower limits of dosage with needles.

One group of nevi has been very troublesome to me—the type in which there already has been some definite necrosis when the patient is first seen. This is not necessarily due to any type of treatment but is a spontaneous necrosis. I have in mind one case I saw recently, an infant three or four months old, with a cavernous type of nevus involving the vulva and extending backwards over the entire perineum, half way up the lumbar region and onto both buttocks. The entire cleft from the vagina back over a distance of several inches showed a definite necrosis, and this extended along several lines laterally. I felt helpless with this type of case, but started some surface treatment. In spite of small doses, the necrosis extended, and the last time I saw the baby the musculature was exposed. I do not know what the eventual result has been. I hope that Dr. Johnston has something to offer in the treatment of this type of nevus.

DR. L. R. SANTE (St. Louis): I would like to ask Dr. Johnston whether or not she follows out the method we heard advocated in Stockholm. She referred to the work at the Radiumhemmet, and I am sure we saw some very good results in the treatment of nevi there. Small doses were given at the start, and after the tumor showed visible evidence of regression the doctors there were rather hesitant to give any more treatment, feeling that time alone would result in

a complete extirpation of the nevus. I would like her to touch, if she will, on the dosage given and the procedure followed.

The case that Dr. Gerber spoke of is almost a counterpart to one I myself had, for which I used relatively unfiltered radiation, filtered only through the steel needles made into a hot plaque. We use this method in small nevi. In very young babies, we endeavor not to exceed twenty to twenty-five or thirty millicurie-hours per square centimeter of surface involved. In adults we go very much higher. We feel that possibly the age of the baby may have something to do with the marked reaction obtained.

I had a similar case of angioma on the vulva of a baby, and there was no necrosis when treatment was begun. The patient received no more than twenty milligram-hours per square centimeter, given all at one dosage. A complete mold of the area was made and the radium was embedded in dental wax. Within three weeks' time the entire area sloughed, much to my concern, and I had visions of all kinds of things happening, but nothing unusual did happen. The slough did not progress, although it looked very angry at the first examination, and within three weeks' time the entire area healed and was almost without scar. It was the most remarkable thing—the speed with which the lesion healed.

I am certainly impressed with what Dr. Stevens and Dr. Martin have said concerning the possibility of the formation of telangiectasis in cases in which the radiation used is unfiltered. In some of the cases of epithelioma which we have treated, we have used relatively unfiltered radiation—radium emanation—put in tubes of only about 0.3 mm. monel metal, and that is pretty low filtration. We now, three or four years later, see the evidence of the beginning of telangiectasis in many of these cases. In the case of a baby from whom an unsightly angioma has been taken off, the patient later developing telangiectasis, it is a question in my mind if we have not done harm instead of good as far as the cosmetic result is concerned.

Dr. R. H. Crockett (San Antonio, Texas): In treating nevi that have a warty appearance, and are red or bluish red in color, with radium, I have found it impossible to benefit the condition by the use of very much filter with the radium. However, by using a one-half strength 10 milligram glazed plaque, with only one-tenth of a milligram of aluminum as filter, I have secured very good results. The elevation of surface and color of the warty nevi have disappeared very satisfactorily after from four to six mild treatments.

Dr. Grier: I might say to Dr. Gerber that it is not at all uncommon for large angiomata to slough without any treatment at all.

Dr. Johnston (closing): In answer to Dr. Gerber's question, I would say that we insert the needles and keep them in position from forty-five minutes to two hours, depending upon the case. We use both 5 and 10 mg. needles; when two 10 mg. needles are inserted into the upper eyelid, as in the case shown by lantern slide, one hour and fifteen minutes' time is given. In some cases in which the radium was placed quite deep into the angiomatous tissue, two hours were given when 10 mg. needles were used. The angioma on the shoulder had a rather severe reaction, but it healed in a short time, leaving a very soft pliable scar. Experience teaches us that smaller doses given at intervals will yield better cosmetic results. A second treatment can safely be given after three months. Some of the cases shown on the screen were treated five and six years ago. I make a point of seeing them once or twice a year.

A MEMBER: How close together were the 10 mg. needles?

DR. JOHNSTON: The needles were spaced from five to ten mm. apart. Dr. Gerber described a case of spontaneous breaking down or necrosis in the center of the lesion. I have never treated a case of that kind, and I have not had a necrosis or breaking down which failed to heal following treatment. A young child with a lesion such as he described would not be a very favorable case for the use of radium.

In answer to Dr. Sante's question concerning the methods at the Radiumhemmet, I would say that I would not follow their methods particularly.

A MEMBER: Do you vary the dosage in a baby or adult?

DR. JOHNSTON: I think that I am a little more cautious as to the amount of radium used and the length of time of treatment in the case of very young babies.

EDITORIAL

M. J. Hubeny, M.D. . . . . *Editor*

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ACHIEVEMENTS OF RADIOLOGY IN THE UROLOGIC FIELD[1]

There is no branch of medicine but that owes a debt to radiology for in some way advancing either its methods of diagnosis or of treatment, and in no one of the medical specialties does this more forcefully apply than in urology. To-day the genito-urinary surgeon would consider his study of a case but half done if roentgenograms were omitted. In the differential diagnosis between urinary and extra-urinary conditions, the opaque ureter catheter, the ureteropyelogram, and the cystogram render errors much less likely. At one time these so-called more intricate procedures were reserved for the complicated cases: to-day we find them being employed as routine. For this reason fewer anomalous states will escape detection. The modern X-ray tube and the incorporation of the Potter-Bucky diaphragm as a part of every cystoscopic table have lent weight to more painstaking investigations. The adoption of harmless solutions in pyelography has added materially to the safety factor in doing this work.

Throughout a period beginning with Tuffier, in 1897, down to the work of Braasch, in 1927, we find many names in our literature on urography—and all are urologists: it is the exception to find the radiologist mentioned. Occasionally one meets the name of Pfahler, but on most rare occasions. Surely we all realize that this valuable addition to our armamentarium was made possible only by the combined efforts of the radiologist and urologist. It is only fitting, therefore, that tribute be paid to members of that specialty of medicine who have aided so materially in advancing urologic diagnosis.

The modesty with which the radiologist has remained in the background during the past thirty years of effort to better visualize the urogenital tract under the X-rays renders it most difficult for the essayist to give proper credit where credit is due. No doubt my listeners know far better than I to whom the homage should be paid. Suffice it to say that urologists realize fully the inestimable value of radiologic opinion. It will probably serve our purposes best if we review briefly some of the conditions that we encounter daily in which such consultations are necessary.

The differential diagnosis of abdominal shadows on films is not always easy. We know, for example, that shadows suspected of being kidney or ureteral calculi may be of other origin. Gallstones, pancreatic calculi, calcified abdominal glands, phleboliths, calcareous deposits in renal tissue, intestinal contents, and appendicular concretions are but a few of the extra-urinary factors that must be reckoned with. Here the opaque ureteral catheter, the pyelogram and the cystogram, when associated with stereographic, anterior-posterior and lateral studies, give the necessary information.

In developmental abnormalities either of the kidney, the ureter, bladder, or urethra, the radiologist, working in conjunction with

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 28–Dec. 2, 1927.

the urologist, daily demonstrates malformations with such uniform precision that many conditions ten years ago considered extremely rare are now passed over as commonplace. I refer particularly to duplications of the renal pelvis and ureter, strictures of the ureter, diverticula in ureter and bladder, and congenital anomalies of the posterior urethra. Fused kidney, congenitally large pelves, apparent renal torsion and ectopic kidney are more frequently reported at present than formerly. Numerous observers have reported two ureters going to a single kidney. This pre-operative finding is obviously of utmost value to the surgeon. We have all heard of cases in which nephrectomy was performed upon the only kidney the patient had.

If we should inquire as to the condition in which the radiologist has been of most value in the diagnosis of urinary lesions, I am sure we would all agree that the recognition of calculi unquestionably claims first place. From the earliest days of X-ray examination the detection of stones in the kidney, ureter, bladder, and urethra has materially aided the urologist in arriving at a prompt and correct diagnosis.

In the study of the genito-urinary tract, calculi in the prostate are visualized. By co-operation with cystoscopic workers opaque media have been introduced into the renal pelvis and ureter, which, apart from outlining these structures graphically, serve for coating calculi not otherwise easy of recognition. The routine maneuver of making lateral films as well as taking the usual anterior-posterior exposure of both kidney areas aids in the differentiation of extra-renal shadows.

This matter of lateral urograms has not, in my opinion, been sufficiently stressed. From personal observation in my own service at the Southern Baptist Hospital, where it is routine to make such exposures whenever shadows are detected in the kidney areas, I have found lateral exposures most valuable, and I commend them to you. We feel that all shadows lying within the plane of the vertebræ or behind the spine are usually renal calculi and those found in front of the spine extra-renal. With the added assistance of the opaque catheter in such instances, the study becomes of still more interest. Stereographic studies of the urinary tract are universally recognized by all X-ray workers for the valuable information they at times impart, yet I cannot but feel the procedure is of secondary value when compared with lateral roentgenographs.

Pyelography is justly esteemed as a diagnostic measure of inestimable value in the differentiation of normal from abnormal development in the renal pelvis and its accompanying calyces. It is impossible for one to visit the scientific exhibits of any representative medical meeting nowadays without being impressed with the many interesting and instructive exhibitions of abnormal findings in the upper urinary tract which so graphically portray lesions impossible of detection by any other means. To me, the art of radiology reaches its heights in these "wonder-pictures."

For advancement along these lines the urologist has, with his usual modesty, taken a lion's share of the credit. That he has worked assiduously over a long period in order that the procedure might be made safe for all, no one questions. The transition through an arduous period, which began with numerous filthy-staining silver suspensions and has ended in the adoption of clear, non-irritating solutions of sodium iodid, marks an onward march of scientific progress of which every American urologist can be proud. Still, throughout all the years of experimentation there was no more loyal supporter nor ardent co-worker than the radiologist. His whole-hearted encouragement to the cystoscopist in the effort to

make pyelography a procedure ready for universal acceptance remains one of the many unread chapters in medical history. Having myself lived through this period I can say in all sincerity that the stimulus given me by my confrères in the X-ray field aided to no small degree in keeping up my enthusiasm. I should feel disloyal if I failed to mention here specifically two men, Henriques and Granger, who, in 1912, made it possible for me to make the first pyelograms ever attempted at Charity Hospital.

Well do I remember the obstacles that appeared in the way of young urologists in those days. We were told that to pyelograph a patient meant sure death—to the patient: that the principles underlying the procedure were unsound. It was alluded to, by many of the wiseacres, as just one more passing fad. To-day we know that an intelligent and comprehensive study of the urinary tract cannot be considered complete unless opaque solutions have been made to cast their shadows on films scientifically exposed by the radiologist.

Nephroptosis is a condition that years ago was not always diagnosed correctly. Many a patient was subjected to major surgery in order to replace a wandering kidney, when, upon lumbar exposure, the kidney was found in its normal position and the tumor proved to be one of intraperitoneal origin. Such mistakes are not made to-day in hospitals where competent radiological and urological consultants serve the staff. Enlargements of the kidney as contrasted with extra-renal tumors of the upper quadrants of the abdomen are easily differentiated by urographic studies. Renal tumors are rarely missed in a cystoscopic room study. Braasch has advanced to the stage where he is able to diagnose the type of tumor present solely on pyelographic evidence. Truly we live in a wondrous age! Year by year we seem to feel that we are approaching ever closer to a medical millennium. There now appears to be little that can be added to our diagnostic armamentarium as applies to urological conditions.

I wish I could say as much for therapy. For, in the attempt to conquer cancer, the medical man seems far indeed from his goal. The employment of radium and deep X-rays has not solved the problem, howbeit much credit is due workers in the radiologic field for their efforts so far. They have demonstrated conclusively just how much we may expect from physical agents. We appreciate with what facility accessible growths are being promptly eradicated by means of surgical diathermy. Still, with inaccessible tumors, which make up by far the majority, we must acknowledge our limitations. I trust that the efforts put forth so far by radiologic experimenters will carry us still further, until ultimately cancer will not be the dreaded scourge it is at present. I firmly believe the radiologist will be the one that will finally lead us out of the darkness into the light. May fate speed the day!

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A lack of the important beta hormone, which controls the water depots of the body and the ability of the tissues to use water and which is in the post-pituitary gland at the base of the brain, may be made up by an artificial supply from animal glands, Dr. Oliver Kamm, of Detroit, Mich., has announced.—*Science Service.*

Two Swiss physicists, Dr. A. Piccard and Dr. E. Stahel, have performed an ether-drift experiment with negative results.—*Science Service.*

MR. E. C. JERMAN RECEIVES DEGREE OF SC.D.

Mr. E. C. Jerman, Director of the X-ray Division, Victor Educational Department, has been given the degree of Doctor of Science by Franklin College, Franklin, Indiana. This information will undoubtedly be of interest to Mr. Jerman's many friends, both in this country and abroad, who have come to a full appreciation of what he has contributed toward the standardization of operative X-ray technic. His experience in this field dates from 1895, when cable messages informed America of Prof. Roentgen's great discovery. At that time Mr. Jerman was engaged in the manufacture of static machines and other electrical devices for therapeutic purposes, and became intensely interested in reading the newspaper reports and the scientific journals, pertaining to this discovery. Everything was available with which to try the experiment, except a Crookes tube, but this was obtained as soon as it was possible to make the importation. It was on the night of March 16, 1896, that Mr. Jerman and three of his associates made their first experiments, which were concluded at 3 o'clock the next morning. They succeeded in obtaining a radiograph of the hand in a 30-minute exposure, sufficient to show the shadows of the bones of the fingers.

Mr. Jerman has participated in the development of the X-ray, his interest being largely on the technical side of the equipment used in the X-ray laboratory. Radiologists in practically every country of the world have benefited by his instruction and are able to attest to his ability to impart to others a knowledge of the fundamentals of operative X-ray technic. It is in recognition of his many contributions to the field of X-ray science, that the Degree of Doctor of Science has been conferred on Mr. Jerman by his *alma mater*.

EASTMAN SCHOOL OF X-RAY PROCESSING

The Medical Division of the Eastman Kodak Company, at Rochester, New York, has established a new Educational Department, where X-ray technicians may acquire basic training in the photographic phases of their work.

The physician, the surgeon, or the dentist making X-ray examinations is urged to avail himself of the facilities of this department for the free instruction of his technician in X-ray film processing.

There are exact and reliable methods of processing radiographs that insure the preservation of all significant details recorded on the film, and that also afford a constant check upon exposure technic. These methods are not difficult to follow, and any technician may learn them in the short course now being offered by the Eastman Kodak Company. This course is repeated at frequent intervals and is open without charge to any technician, male or female, who is employed by an ethical medical or dental practitioner. Medical men themselves are, of course, welcome at all times to attend any of the classes.

Instruction in the school for X-ray technicians is given by the staff of the Medical Division of the Eastman Kodak Company. It is confined primarily to the processing of radiographs; exposure technic and interpretation are discussed only in their relation to the development of the negative.

The course is of five days' duration, which means intensive application on the part of the student. Although the course is limited to X-ray processing, students interested in clinical photography, photomicrography, or the making of medical motion pictures will have the opportunity to obtain information on these subjects in special conferences with members of the Kodak staff. A complete library on X-ray science and on various branches of technical photography is also available for the use of the students.

As previously stated, the course is free. The only expenses in connection with attendance are the student's railroad fare and living expenses while in Rochester. Through the co-operation of the Rochester Hotel Men's Association, provisions will be made for satisfactory and economical accommodations. Every care is taken to insure the comfort and welfare of those attending, and there are special provisions for women students.

For effective instruction, the classes in X-ray processing are kept small. It is advisable, therefore, to apply early for a reservation. To do so, it is only necessary to apply for, fill out, and return an enrollment blank, underlining the course date that best suits your convenience. You will be notified at once whether your representative can be accommodated in the course given on that date. Please co-operate by filling out the enrollment form as fully as possible.

ABSTRACTS OF CURRENT LITERATURE

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Injection of Air by the Lumbar Route in Diagnosis and Treatment. J. Norman Petersen. Can. Med. Assoc. Jour., August, 1928, XIX, 184.

This procedure consists of the radiographing of the basilar and pontine areas of the brain in which the cerebrospinal fluid has been replaced by air, through the lumbar puncture route. This is in contrast with ventriculography in which the fluid is drawn off and air injected by puncture of the ventricles. The author gives the detailed technic of the operation.

His conclusion is that this is a useful method of examination and treatment. However, it requires expert manipulation and interpretation, and in the presence of contra-indications becomes a dangerous procedure.

L. J. CARTER, M.D.

Radium Treatment of Primary Carcinoma of the Breast. Geoffrey Keynes. Lancet, July 21, 1928, CCXV, 108-111.

This article is interesting from the standpoint of treating operable cancers of the breast with radium. The author uses two lengths of needles, one 4.8 cm., one 3.2. The longer one contains 3 mgs. of radium element and the shorter 2 mgs., and they are made of platinum 0.5 mm. in thickness. The longer needles are used for implanting in the primary tumor, into the axilla beneath the pectoralis major muscle, and into the axilla proper beneath the glenoid and immediately beneath the clavicle. The shorter needle is used in the supraclavicular space and in the rib interspaces immediately contiguous to the tumor. The needles are left for a period of from one week to ten days. They are both inserted and removed under gas oxygen anesthesia. At the time of removal a biopsy is done.

From 1924 until the end of June, 1928, 42 patients have been treated in this manner. They are classified as follows: Inoperable 17, operable 22, doubtful 3. Of the inoperable class six died of metastases and none of them lived more than nine months after treatment.

There are thirteen listed as apparently cured, one for four years, one for three years two months, one for two years two months, one for two years, and the others for from two years to eight months.

The report is quite complete and includes roentgenograms showing needles in place, also photographs of patients before and after treatment. As there is no patient reported as well for more than four years without recurrence this paper must be considered as a more or less preliminary report, and it is hoped that the author will again report his series when a reasonable number have passed the five-year period.

H. J. Ullmann, M.D.

The Roentgen-ray Diagnosis of Infantile Scurvy. Ralph S. Bromer. Am. Jour. Roentgenol. and Rad. Ther., February, 1928, XIX, 112.

The roentgen-ray findings in cases of infantile scurvy may be divided into four stages. The first stage (the clinically early or latent type) shows constantly a dense calcified edge or ring about each epiphysis, while the center of the epiphysis presents a "ground glass appearance." The shaft likewise shows a "ground glass appearance," the cortex shows "pencil-point thinning," and a broadened dense zone of temporary calcification at the very end of the shaft or metaphysis is to be seen. The second stage shows two additional roentgenographic signs: A zone of decreased density appears just behind the broadened zone of temporary calcification, and lateral spurs or projections at the diaphyseal ends, the first sign of hemorrhage, may be seen. In the third stage the well recognized X-ray sign of subperiosteal hemorrhages is found. The fourth stage is the stage of absorption of hemorrhage, with repair of all of the scorbutic lesions. The author has noted a persistence of periosteal thickening, as evidence of the former subperiosteal hemorrhage, after a lapse of five years.

In the series of 56 cases reported, 13 showed first-stage findings, with only 5 having been definitely diagnosed clinically; 33 were in the second stage; 9 in the third stage, and one case when first studied was already in the healing or fourth stage. Wimberger's sign, or the "ground glass appearance" of the epiphysis, with its dense edge or ring, is stressed by the writer as being the most constant and reliable finding in the early course of the disease.

J. E. Habbe, M.D.

Compression Myelitis. William A. Smith and Charles E. Dowman. Am. Jour. Surg., February, 1929, VI, 151.

Lesions encroaching on the spinal canal may cause compression myelitis. These lesions are divided into: First, extra-spinal diseases; second, lesions of the spinal column; third, lesions within the spinal canal. The extra-spinal diseases are aneurysm, producing vertebral erosions, spinal and extra-spinal tumors invading the spinal canal through direct extension. The spinal diseases are tuberculosis and various spinal deformities, neoplasm, arthritis, osteomyelitis, and various types of injuries. The lesions within the spinal canal include tumor, abscess, newgrowth, etc.

In making the diagnosis, the diagnostic aids used are: First, history; second, neurological examination; third, roentgen-ray examination; fourth, spinal fluid examination; fifth, Queckenstedt's test, and, sixth, the intra-spinal injection of substances to cast a shadow on the roentgen-ray film.

The authors present six cases of compression myelitis caused by neoplasms of different types and locations.

H. P. Doub, M.D.

Diverticula of the Colon: Pathological and Clinical Study. Robert Mailer. Lancet, July 14, 1928, CCXV, 51.

The author gives the results of a thoroughly conducted pathological and clinical study in a series of fifty-three specimens. The sites of diverticular formation as determined by this study correspond closely with those determined by roentgen examination. A complete

description of the gross and microscopic pathology is given. The author found the situation of diverticula in relation to the circumference of the bowel markedly constant: they most often appear between the mesocolic and the anti-mesenteric longitudinal bands, the diverticula being definitely related to the afferent mesenteric vessels.

In the series studied associated diverticula were found in the duodenum in four cases, in the jejunum in two cases, and in the bladder in two cases. The author does not believe that this co-existence is common enough to favor a congenital etiology, and believes that the congenital type is rare.

As regards the relation of diverticulitis and carcinoma the author believes that the high incidence of diverticula in persons over the age of 45, with the resulting degenerative changes in the parts involved, has a definite bearing on the occurrence of carcinoma at this age.

Tuberculosis of the sigmoid was found in two cases of sigmoid diverticulitis. Attention is drawn to the similarity in appearance of hyperplastic tuberculosis and diverticulitis of the sigmoid. The clinical features of the various stages of diverticulitis are well described on the basis of a study of one hundred cases. The author concludes with the treatment indicated, advising surgery in severe cases or wherever obstructive symptoms are present.

M. J. Geyman, M.D.

Electrodesiccation and Electrocoagulation in Neoplastic and Allied Diseases of the Oral Cavity and Adjacent Parts: Clinical, Physical, Historical, and Photographic Studies Based upon 20 Years' Experience. William L. Clark. Am. Jour. Surg., March, 1929, VI, 257.

The author first describes the technic employed in the two methods and their use in connection with radiotherapy. He believes that malignant disease within the mouth and adjacent parts, while always a serious affection, is not always hopeless if treated by the combination of these methods. In certain instances cervical lymph nodes are surgically resected, but never before the primary malignancy has been destroyed or inhibited. He usually treats the primary lesions by the electrothermic method, and the metastases by irradiation.

This paper is well worth careful study in its entirety.

H. P. Doub, M.D.

Investigations on Very Soft Roentgen Rays, So-called Grenz Rays. B. Rajewsky and G. Gabriel. Strahlentherapie, 1928, XXX, 308.

A recalibration of the kilovoltmeters of some commercial apparatus designed for the production of roentgen rays in the range from 8 K.V. to 12 K.V. revealed a discrepancy between different makes. For research purposes, it is necessary, therefore, to measure the potential at the tube terminals. Biophysical studies with 8, 9, and 12 K.V. convinced the authors that it is not necessary to use a potential of 9 K.V. only, because neither of the investigated radiations showed any specific effects. The skin capillaries respond to rays of such long wave length, that an erythema will always appear if enough radiation reaches the blood-vessel-bearing layer. For 9 K.V., 15 cm. F.S.D., the average erythema corresponded to about 225 *R*.

E. A. Pohle, M.D., Ph.D.

Our Experience with X-ray Therapy of Carcinoma of the Cervix. M. Bolaffio. Strahlentherapie, 1928, XXIX, 453.

In the gynecological clinic of the University of Rome, radiation therapy of carcinoma of the uterus was started in 1914; mesothorium was used exclusively until 1920. In 1926, 16 (or 7.34 per cent) out of 218 patients treated were alive. Beginning in 1920, X-ray deep therapy was used, many times combined with an application of radium. The author's statistics show that this combination of X-ray and radium gave the best results. A very interesting curve is presented showing the per-

centage of recurrence in the years following irradiation. If compared with his operative results, the author concludes that operation on carcinoma of the cervix is the method of choice. Radiation is permissible only when operation is impossible or too dangerous, except in a very small carcinoma which can be entirely eliminated by radium.

E. A. POHLE, M.D., PH.D.

The Calibration of X-ray Dosimeters with Radium. Hermann Behnken and Robert Jaeger. Strahlentherapie, 1928, XXIX, 483.

The advantages of the absolute unit, one Roentgen, in defining X-ray doses, and some of the errors which may occur when small ionization chambers are checked by too small amounts of radium are pointed out. If the radium check of a small ionization chamber is to be reliable, more than ten milligrams of radium element are required. Large chambers may be checked by very small amounts of radium by using Alpha and Beta radiation. The current standard of Behnken, consisting of uranium oxide, is an inexpensive and very efficient method for that purpose.

E. A. POHLE, M.D., PH.D.

A Roentgen-ray Study of a Group of Long-distance Runners: With Special Reference to the Effects of Exercise on the Size of the Heart. J. T. Farrell, Jr., P. C. Langan, and Burgess Gordon. Am. Jour. Med. Sci., March, 1929, CLXXVII, 394.

A roentgenographic study of a group of long-distance runners was made to determine the effect of prolonged effort on the heart, lungs, bones, and blood vessels. The lungs were found essentially normal. The bones, except for certain osteo-arthritic changes, were normal. The blood vessels were visualized only in the older runners. In 13 runners, the hearts appeared smaller than normal; in 5 the hearts were within normal limits, and in 5 the hearts, according to prediction, showed an increase in size. According to the so-called cardiothoracic ratio, only one heart was increased in size.

The data as a whole suggest that the immediate effects of long-distance running are inconsequential, since all the changes noted may be found in individuals of similar ages without symptoms.

ROBERT A. ARENS, M.D.

Radiological or Surgical Treatment of Uterine Carcinoma. J. Heyman. Strahlentherapie, 1928, XXIX, 407.

The author presents a very careful evaluation of all statistics available in the world literature. He comes to the conclusion that no definite decision is possible at present regarding the superiority of either operation or irradiation. A comparison on the basis of inoperable cases is impossible and there are not enough operable cases treated by radiation alone to permit final conclusions. It is safe to assume, however, that so far surgery has not produced better results than radiotherapy.

E. A. POHLE, M.D., PH.D.

Contribution to the Radium Treatment of Skin Carcinoma, with Statistical Notes. Fritz Dautwitz. Strahlentherapie, 1928, XXIX, 634.

The treatment of skin carcinoma by radium is warmly recommended as the method of choice. A comparison with surgical results reveals the superiority of radium. This paper is well illustrated and presents a number of case histories, followed by a very complete bibliography. One to 3.5 milligrams of radium per square centimeter were used without filter, through rubber dam, through 0.1 to 0.2 silver, or through 0.1 to 1.0 lead. Beta radiation seemed always to be effective. Between 1911 and 1926, 186 cases were treated: 108 patients (Group I) received radium primarily and only 78 cases (Group II) had had roentgen rays, radium, or surgery somewhere else, first, without success. Ninety-seven were males and 89 were females. In the first group there were 70.4 per cent cures after three years and 38.9

per cent cures after from five to fifteen years. In the second group, there were 50 per cent cures after three years and 19.2 per cent cures after from five to fifteen years. This illustrates very clearly that the prognosis in skin carcinomata which are unsuccessfully treated first or recur is less favorable than in those which are primarily treated by radium, followed immediately by a cure.

E. A. POHLE, M.D., PH.D.

On the Technic of Roentgen Therapy of Surgical Tuberculous Diseases. Josef Palugyay. Strahlentherapie, 1928, XXX, 397.

During the past four years, the author has observed over 360 cases of surgical tuberculosis which were treated by X-ray. He contends that an improvement in the curative results can not be gained by increasing the applied dose above 5 per cent E.D. on the surface or 1 to 5 per cent E.D. in the diseased tissue (radiation: 180 K.V., 0.5 Zn. + 1.0 Al.). The technic in treating lymph glands, bones and joints, tendon sheaths, peritoneum, ileum and cecum, kidneys and ureter, bladder, and male genital organs is discussed in detail and results are given. Thirty per cent of the cases were cured and the disease arrested or improved in 50 per cent. Sometimes X-ray therapy was combined with exposure to the mercury vapor lamp and As. injections. Four to six series of X-ray treatments were given over a period of seven months. A very extensive bibliography concludes the article.

E. A. POHLE, M.D., PH.D.

Non-malignant Tumors of the Duodenum: Report of Two Cases. Ross Golden. Am. Jour. Roentgenol. and Rad. Ther., November, 1928, XX, 405.

The author observed roentgenologically two cases of benign tumors of the proximal duodenum, one being a large polyp composed of mucous cells, and the other a smaller adenoma composed of Brunner's glands. The smaller tumor produced a symptom-complex strongly suggestive of duodenal ulcer but on gastro-intestinal X-ray examination a vacuolated area could be demonstrated lying centrally in an otherwise normal duodenal bulb, and a normal six-hour evacuation of the stomach took place. The roentgen diagnosis was probable polyp.

The other case reported was one clinically of long-standing dyspepsia with recent weight-loss of forty pounds in four months, associated with inability to retain food. Roentgen studies revealed marked spasm of the antral portion of the stomach, which persisted in the presence of belladonna to such a degree that the duodenum was never satisfactorily visualized, but, despite the marked spasm, no six-hour retention occurred. The writer believes the absence of any six-hour retention to be an important aid in the diagnosis of non-malignant duodenal tumor in those cases where the fairly characteristic filling defect in the duodenal bulb is demonstrable.

J. E. HABBE, M.D.

Our Experience with Gonorrheal Arthritis. Sepp Grauer. Strahlentherapie, 1928, XXIX, 303.

Gonorrheal arthritis was treated by roentgen rays, three to four surface doses of 3 to 4 H each through fields of 15 × 15 cm. being applied. For small joints, the F.S.D. amounted to 30 cm.; for larger joints, 40 cm. Filter: 4 mm. Zn. + 2 mm. Al.; minimum wave length 0.1 Ångstrom. It is not advisable to go below 25 per cent E.D. per field. The treatment may be repeated at intervals of from several days to one week. There is almost no contra-indication to this therapy except perhaps ankylosis. In acute and sub-acute cases, considerable relief almost immediately follows the treatment. In the author's opinion, the results are permanent.

E. A. POHLE, M.D., PH.D.

An Attempt with Roentgen Therapy in Psychiatric and Neurologic Diseases of Childhood. W. F. von Wieser. Strahlentherapie, 1928, XXXI, 147.

This article is not suitable for abstracting but should be studied by all means in the

original because it discusses a problem which might prove to be of enormous value. Fourteen groups of psychiatric or neurologic diseases in childhood are discussed and indications for X-ray therapy of each group are given. In the author's hands, the method has been quite successful.

E. A. POHLE, M.D., PH.D.

Surgical Diagnosis and Treatment of Lung Abscess. Adrian V. S. Lambert. Laryngoscope, April, 1929, XXXIX, 224.

In this article the author has outlined the rôle of the surgeon in the treatment of lung abscess. He goes on to outline the proper treatment, the proper time for drainage, and the counter-indications. He reports excellent results, as high as 90 per cent of the patients being restored to perfect health. He goes on to describe why an early operation or a late operation is so very often fatal to the patient, and emphasizes the fact that there should be the closest co-operation between the internist, surgeon, bronchoscopist, and radiologist so that the abscess may be properly localized and the proper time for drainage be selected.

B. C. CUSHWAY, M.D.

On the Influence of Small Doses of Roentgen Rays Directed to the Ovaries upon the Offspring of White Mice. A. I. Krupski and M. F. Eisenberg. Strahlentherapie, 1928, XXX, 527.

The ovaries of 40 mice four weeks of age were exposed to graded doses of roentgen rays. Twelve, 24, and 36 per cent E.D. were applied over the whole lower body if both ovaries had to be exposed; otherwise a field of 1 cm. diameter over one ovary only was irradiated. It appeared that the maximal dose of 36 per cent E.D. was far from being the castration dose for white mice. No injury to the offspring into the F_3 was observed. Small doses to the ovaries can, therefore, be recommended in human therapy. The authors also observed three women who became pregnant shortly following small doses to the ovaries; they all had normal deliveries and the three children born were normal. The authors further studied three children of X-ray technicians who had been working in X-ray laboratories for many years. These children were without any obvious abnormalities.

E. A. POHLE, M.D., PH.D.

Roentgen Findings in Neuroblastoma: Report of Two Cases. Carye-Belle Henle. Am. Jour. Roentgenol. and Rad. Ther., November, 1928, XX, 414.

Two cases of neuroblastoma, one arising from the paravertebral sympathetic plexus in a boy aged 2½ years, and the other occurring with the primary tumor in the adrenal in a boy aged 7, are reported, in both of which rather characteristic skull changes were observed in the roentgenograms. In each case there was a wide separation of the coronal suture, due to metastatic nodules in the brain substance. Each case also showed a porous appearance of the bones throughout the vault due to pin-point areas of rarefaction.

J. E. HABBE, M.D.

Determination of the Reflection of Ultraviolet Rays by Metals with Cadmium Cell and Electrometer. A. Ruttenauer. Strahlentherapie, 1928, XXX, 579.

The reflection of ultra-violet rays from metals has been investigated with a cadmium photo-electric cell. A combination of filters was used which rendered the cell most sensitive to lambda equal to 2,950 Ångströms. It appeared that this line was reflected best by mercury (82.5 per cent); then followed cadmium (74.5 per cent), beryllium (70.1 per cent), iron (50 per cent), and nickel (42 per cent).

E. A. POHLE, M.D., PH.D.

Contribution to the Question of Standardizing the Small Ionization Chamber. R. Jaeger. Strahlentherapie, 1928, XXX, 567.

The author suggests that an agreement should be reached on a standard ionization chamber of the thimble type for measurements in the X-ray laboratory. Such chambers should be independent of the wave length

within the range used in therapy; the air volume and wall material should be uniform; the material on the inner walls of the chamber should be an excellent conductor; such a chamber should be independent of direction; the shadow effect of the chamber carrier should be avoided; last, not least, such a chamber ought to be mechanically solid. Experiments have convinced the author that it is possible to manufacture such a chamber on a quantity production basis.

E. A. POHLE, M.D., PH.D.

Roentgen Therapy of Purpura Hemorrhagica Menstrualis. G. H. Schneider. Strahlentherapie, 1928, XXX, 503.

A case of purpura hemorrhagica is described in which the symptoms always appeared with the menstrual period. An intensive X-ray exposure of the spleen (30 per cent E.D. effective in the spleen) brought only temporary relief. Application of the full sterilization dose, followed by amenorrhea, led to a cure.

E. A. POHLE, M.D., PH.D.

The Preservation of the R-unit. H. Hase and H. Küstner. Strahlentherapie, 1928, XXIX, 745.

A series of measurements have been carried out which show that radium control of ionization instruments with a large chamber is reliable. The probable error for a single control with Beta radiation is 3.3 per cent and with Gamma radiation is 0.65 per cent.

E. A. POHLE, M.D., PH.D.

Hysterosalpingography and the Diagnosis of Ectopic Pregnancy. M. Pierce Rucker and L. J. Whitehead. Am. Jour. Roentgenol. and Rad. Ther., November, 1928, XX, 431.

The authors discuss the reliability of the hysterosalpingogram in the diagnosis of ectopic pregnancy. The typical findings are said to consist of a rounded, globular form of the uterine lumen shadow due to "pregnancy atony," with no filling defect to indicate the presence of an intra-uterine ovum, and an irregularly filled tube on one side. In the authors' case one tube filled normally, the other was completely obstructed, and there were many filling defects in the uterus. Operative findings disclosed a ruptured left tube; the filling defects in the uterus were apparently due to adherent blood clots.

J. E. HABBE, M.D.

Regarding Superficial X-ray Therapy with Smallest Dose. H. Fuhs and Josef Konrad. Strahlentherapie, 1928, XXIX, 230.

Following Thediring, the authors treated a variety of skin diseases (alopecia, sycosis, eczema, psoriasis, acne, lupus vulgaris) with very small doses of roentgen rays. A single exposure amounted to one-tenth to one-fourth to one-half H. The technic is expressed in a rather complicated code, for which no key is given for deciphering. While not all diseases responded to this type of treatment, it is emphasized that the possibility of an over-dose is rather small. No results were seen when exposing the spleen in cases of furunculosis, urticaria, and psoriasis. This indirect method of treatment is, therefore, not recommended by the essayists.

E. A. POHLE, M.D., PH.D.

The Effect of Irritation of the Colon on the Emptying Time of the Stomach. R. T. Monroe and E. S. Emery. Am. Jour. Med. Sci., March, 1929, CLXXVII, 389.

Because of the numerous instances in the literature suggesting that pathology or irritation in the colon or ileocecal region may affect the gastropyloric mechanism, resulting in a change in the emptying time of the stomach, the writers undertook this experiment, using dogs. They produced a simple but severe chemical irritation of the mucous membrane of the colon by means of turpentine and found that this produced no change in the emptying time of the stomach.

ROBERT A. ARENS, M.D.

Experimental Investigations on the Tongues of Frogs Regarding the Effect of Different Qualities of Radiation on the Blood Vessels. R. Motojima. Strahlentherapie, 1928, XXX, 343.

The effect of X-rays, radium, thorium X, and ultra-violet rays on the blood vessels of the tongues of frogs was studied. It manifested itself in dilatation of the vessels, reduced speed of the blood stream, stasis, diapedesis, and edema. While these observations were made following exposure to all types of radiation used, there were differences in the time-curve of the reaction. For instance, the response to ultra-violet rays appears the quickest and also disappears after the shortest interval.

E. A. POHLE, M.D., PH.D.

On the Effect of Cathode Rays on Erythrocytes (Blood Agar Plates). W. Hausmann and W. E. Pauli. Strahlentherapie, 1928, XXX, 350.

If blood agar plates are exposed to cathode rays, hemolysis appearing in ring form has been observed by the authors. The erythrocytes in the center of this lighter ring are not hemolyzed; they are resistant to saponin.

E. A. POHLE, M.D., PH.D.

A Large Sarcoma Cured by Roentgen Rays. Felix Gál. Strahlentherapie, 1928, XXXI, 88.

The history is related of a woman 49 years of age who was admitted to the hospital in September, 1924. She stated that three years previously her abdomen began to enlarge and it increased in size until a year before the present admission. She had an attack of fever, and pus was discharged from the vagina. The size of the abdomen decreased, after which followed a nine-months period of amenorrhea. She then began to lose weight, had pain in the lower abdomen and lumbosacral region, and suffered shortness of breath. Examination showed that the tumor extended from the xiphoid process of the sternum down to the uterus. Biopsy verified the clinical diagnosis of sarcoma. Because of almost constant bleeding, a curettage was done, which stopped the hemorrhage. Eighteen days following the operation, X-ray deep therapy was given to the pelvis, followed by three more treatments at five-week intervals. In June, 1925, the uterus was the size of a man's fist. The patient has gained fifteen pounds and at the time of the report felt perfectly well.

E. A. POHLE, M.D., PH.D.

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